CHAPTER 20
PULMONARY ASSESSMENT

INTRODUCTION

Background

Apart from local irritative symptoms occurring in industrial accidents, there is no clinical evidence that the human lung is a target organ for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD, or dioxin) toxicity. A single case of hypersensitivity pneumonitis was described in a Vietnam veteran occupationally exposed to herbicides (1), though there was no scientific basis to support a causal relationship to TCDD. The respiratory failure that has been reported in rare cases of extreme phenoxy herbicide intoxication appears to be related to central nervous system depression rather than primary pneumotoxicity (2,3).

Research into the pulmonary toxicity of dioxin in laboratory animals has focused on the physicochemical properties of the cytosolic aryl hydrocarbon (Ah) receptor and the cytochrome P-450 enzyme system in mice (4), rats (5,6), and rabbits (7-11).

Several lines of research have heightened interest in the possibility that TCDD might cause pneumotoxicity in man. In one study (12), cytosol preparations were examined from human lung tissue specimens obtained at surgery. Only 10 of 53 specimens had detectable Ah receptors, and those were at concentrations far less (10% to 30%) than those found in lung cytosols from laboratory animals. In mice, the induction of cytochrome P-450 enzymes by TCDD in lung was found to be similar to that in liver (13). In rats (14,15), the intratracheal administration of TCDD was associated with significant dose-related increases in hepatic enzymes as well, establishing the transpulmonary absorption of dioxin and hence, the potential for pneumotoxicity.

Lung disease has been included infrequently as a clinical endpoint in epidemiologic studies of humans exposed to phenoxy herbicides. In one report (16), standard pulmonary function tests were included in clinical examinations of 367 employees 30 years after an industrial explosion associated with high-level exposure to 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) and, by contamination, to TCDD. Although tissue levels were not available, 55 percent of the exposed cohorts developed chloracne, testimony of the severity of exposure. Alone among the objective laboratory indices, pulmonary function as assessed by the forced expiratory volume, expelled at 1 second (FEV_1) percent-predicted values was significantly ($p=0.0005$) compromised in the exposed cohort of current smokers but not in former smokers or in those who had never smoked.

In a more recent report (17), the authors investigated the prevalence of chronic respiratory disease in a cohort of 281 workers occupationally exposed to TCDD in chemical factories. The body burden of dioxin was objectively determined by serum TCDD levels with a mean level of 220 ppt in the exposed cohort versus 7 ppt in the controls. No significant differences were documented in the historical incidence of respiratory disease or in the standard indices of lung function in the exposed cohort relative to the controls. In the most recent reports of the Air Force Health Study (AFHS) (18,19), no significant differences were found between the Ranch Hand and Comparison cohorts in most historical, physical examination, and pulmonary function indices. As a non-specific exception, in the 1987 serum dioxin study, for a physical examination variable thorax and lung abnormalities, Ranch Hands in the low and high current dioxin categories exhibited higher percentages of abnormalities than Comparisons.

Although several animal experiments have documented the occurrence of lung cancers associated with TCDD toxicity in rats (20) and in mice (21), several large-scale epidemiologic studies in humans exposed occupationally (22,23), as a consequence of industrial accidents (24,25), or by military service (18,19,26-28) found no increase in the occurrence of lung cancer in populations at risk. In one report, Marine Vietnam veterans were found to be at increased risk for the development of lung cancer (29). A more recent proportionate mortality study conducted by the Veterans' Administration reviewed the data and concluded that the apparent increased risk might have been related to a lower than expected mortality from lung cancer in the control group of Marines that did not serve in Vietnam (30).

Summary of Previous Analyses of the Air Force Health Study

1982 Baseline Study Summary Results

The 1982 Baseline examination explored historical pulmonary disease by questionnaire and active pulmonary function by standardized spirometric technique. These areas were of significant interest because of suggested operational inhalation of Herbicide Orange by all Ranch Hand enlisted flyers and enlisted groundcrew.

The questionnaire revealed no group differences for historical diagnoses of tuberculosis and fungal infections, pneumonia, cancer, or chronic sinusitis and upper respiratory disease. At the physical examination, the unadjusted means for FEV_1 (percent predicted), forced vital capacity (FVC), and the ratio of FEV_1 to FVC were almost identical between Ranch Hands and Comparisons. Adjusted mean values were not calculated due to significant interactions (group-by-age for FEV_1 and FVC, group-by-smoking for the ratio of FEV_1 to FVC).

Detailed exposure analyses showed two significant associations in the enlisted flyer and enlisted groundcrew strata, but neither was indicative of a linear dose response. Attempts to adjust the means of the pulmonary function values for age and smoking revealed several interactions, but results were essentially negative. Overall, there were no pulmonary diseases, pulmonary function data, or associations of concern.

1985 Followup Study Summary Results

Because of the essentially negative pulmonary analyses from the Baseline examination, pulmonary function (spirometric) studies were not performed during the 1985 followup examination. Collection of pulmonary data was limited to a questionnaire history of respiratory disease, physical examination of the thorax and lungs, and pulmonary abnormalities detected on a routine chest x ray. Mortality due to respiratory disease also was evaluated.

There were no significant group differences found for reported history of asthma, bronchitis, pleurisy, or tuberculosis based on the unadjusted analyses. Adjustments for age and lifetime smoking did not alter the findings of group similarity, although there was a significant group-by-lifetime smoking interaction for pleurisy and tuberculosis.

Similarly, there were no significant group differences in the unadjusted analyses for the radiological and clinical respiratory findings of thorax and lungs, asymmetrical expansion, hyperresonance, dullness, wheezes, rales, and x ray interpretations. These findings were supported by the adjusted analyses, although there was a group-by-age interaction for rales. Also, the exposure index analyses revealed no consistent dose-response pattern.

1987 Followup Study Summary Results

The pulmonary assessment was based on five self-reported respiratory illnesses, seven clinical observations, and eight laboratory measurements. No evidence of an herbicide effect was detected in the assessment of the reported respiratory illnesses. The health of the two groups was reasonably comparable based on the clinical and laboratory variables, although Ranch Hands had a significantly higher percentage of thorax and lung abnormalities on examination than did Comparisons, based on the unadjusted analysis, and a marginally higher percentage after adjustment for covariates. No significant group differences were detected in the adjusted analyses when significant interactions involving group were ignored. Exploration of these group-by-covariate interactions did not reveal a consistent pattern indicating an herbicide effect. The adverse effects of smoking on pulmonary status were evident in all analyses.

Serum Dioxin Analysis of 1987 Followup Study Summary Results

In general, there was no association between initial dioxin and the discrete variables. For the continuous variables, however, there appeared to be a negative association with initial dioxin, especially under the maximal assumption. The associations with current dioxin did not differ significantly between the two time strata for any of the variables, under either assumption. In the categorized current dioxin analyses, the percentage of abnormalities did not differ significantly among the four current dioxin categories for any of the questionnaire and physical examination variables, except under the adjusted analysis of thorax and lung abnormalities. In this case, Ranch Hands in the low and high categories had a higher percentage of abnormalities than did Comparisons in the background category; but Ranch Hands in the unknown category had a lower percentage of abnormalities than did Comparisons in the background category. For the continuous variables, the means differed among the current dioxin categories. For FVC, FEV_1, and forced expiratory flow maximum (FEFmax), the mean for the Ranch Hands in the unknown category tended to be greater than the mean for the Comparisons in the background category, but the means for the low and high categories were less than the mean for the background category. In the analysis of the ratio of observed FEV_1 to observed FVC, this trend was reversed.

In the longitudinal analysis of the ratio of observed FEV_1 to observed FVC, there was a significant positive association with current dioxin and a significant difference among the current dioxin categories.

In summary, the historical, physical examination, and laboratory data analyzed in the 1987 serum dioxin followup study revealed no evidence for an increased occurrence of pulmonary disease in the Ranch Hand cohort in relation to the body burden of dioxin. Analysis of two laboratory variables, FVC and the ratio of observed FEV_1 to observed FVC, yielded results that were consistent with subtle dose-response effects related to the body burden of dioxin in Ranch Hands. Body habitus and, more specifically, percent body fat may play a role in these associations between dioxin and pulmonary function indices.

Parameters for the Pulmonary Assessment

Dependent Variables

The Pulmonary Assessment was based on questionnaire, physical examination, and laboratory data collected at the 1992 followup examination.

Medical Records Data

In the self-administered family and personal history section, each study participant was asked whether he had ever experienced the following conditions: asthma, bronchitis, or pneumonia. This self-reported information was combined with information from the 1992 physical examination, the 1985 and 1987 questionnaires and physical examinations, and the Baseline questionnaire and examination and was subsequently verified by a review of the participant's medical records. These three variables were individually analyzed as measures of the pulmonary health status of each participant. Participants with occurrences of asthma, bronchitis, or pneumonia before duty in SEA were excluded from the analyses of these variables.

Physical Examination Data

Part of the Pulmonary Assessment was based on the results of the physical examination of the thorax and lungs. A composite variable, thorax and lung abnormalities, was constructed based on the presence or absence of asymmetrical expansion, hyperresonance, dullness, wheezes, rales, or chronic obstructive pulmonary disease, as well as the physician's assessment of abnormality. This variable was coded as "abnormal" if any of these conditions were present and "normal" if none of these conditions were present. No participants were excluded for medical reasons from the analysis of this variable.

Laboratory Examination Data

The assessment of the laboratory examination data included the analysis of pulmonary abnormalities detected on a routine chest x ray. This variable was coded as "normal" or "abnormal." The assessment also included the analysis of pulmonary physiologic data collected during the physical examination employing standard spirometric techniques.

Numerous indices were derived including FVC—a measurement of the amount of air in liters expelled from maximum inspiration to full expiration, and FEV_1 in liters—an index derived from the FVC that quantifies the amount of air expelled at 1 second. The values used for these variables were the percentages of predicted values rather than the actual volume or flow rate. The calculations of these percentages included an adjustment for age and height, as prescribed by the American Thoracic Society. The Scripps Clinic and Research Foundation (SCRF) laboratory used the same predictive values regardless of race. For these indices, lower values indicated greater compromise in the lung function. In addition, the ratio of observed FEV_1 to observed FVC was calculated as an index reflective of obstructive airway disease. These variables were analyzed as continuous variables.

Loss of vital capacity and obstructive abnormality were classified as none, mild, moderate, or severe and were analyzed as part of the Pulmonary Assessment. Results judged to be between none and mild were classified as "mild" for all analyses. A similar methodology was used for results between mild and moderate (i.e., classified as "moderate") and between moderate and severe (i.e., classified as "severe"). Due to the low frequencies in the moderate and severe categories, these two categories were combined in the analysis as necessary.

As a guide for determining abnormal pulmonary function, readings below the 95th percentile were considered abnormal for FVC and FEV_1. For men older than 36 years of age, the corresponding percent predicted is 74 percent for the FVC and 73 percent for the FEV_1. An FVC or FEV_1 below 40 percent of that predicted was considered severely impaired, as recommended by the American Thoracic Society. The division between mild, moderate, and severe impairment was arbitrarily defined by dividing the interval between severe impairment and the lower limit of normal into two equal bands. That is, the cutpoint between mild and moderate impairment was at 57 percent of the predicted value. Although the ratio of observed FEV_1 to observed FVC and the appearance of the flow volume curve are useful to the physician interpreting the test, there was insufficient data to support arbitrary lower limits of normal or cutpoints to classify impairment as mild, moderate, or severe.

No participants were excluded for medical reasons from the analysis of these variables.

Covariates

The effects of age, race, military occupation, current cigarette smoking (cigarettes/day), lifetime cigarette smoking history (pack-years), body fat (percent), and exposure to industrial chemicals (yes, no) were used in adjusted statistical analyses evaluating the pulmonary dependent variables. Current cigarette smoking was used as a candidate covariate for the physical examination and laboratory variables. Current cigarette smoking and lifetime cigarette smoking history were based on self-reported questionnaire data. For lifetime cigarette smoking history, the respondent's average smoking was estimated over his lifetime, assuming 365 packs of cigarettes equal 1 pack-year. The exposure to industrial chemicals covariate represented lifetime exposure based on self-reported questionnaire data from this examination combined with previous examinations.

Age, current cigarette smoking, lifetime cigarette smoking history, and body fat were used in the continuous form for modeling purposes in all general linear models and logistic regression analyses. These covariates were discretized for clarity of presentation (e.g., interaction summaries).

Statistical Methods

Chapter 7, Statistical Methods, describes the basic statistical methods used throughout this report. Table 20-1 summarizes the statistical analyses performed for the Pulmonary Assessment. The first part of this table lists the dependent variables analyzed, the source of the data, the form of the data, cutpoints, the candidate covariates, and the statistical methods. The second part of the table further describes the candidate covariates. Abbreviations used in the body of the table are defined at the end of the table. Table 20-2 provides the number of participants with missing dependent variable and covariate data and those excluded due to pre-SEA conditions.

Analyses of data collected at the 1987 followup study indicated that dioxin was associated with military occupation. In general, enlisted personnel had higher levels of dioxin than officers, with enlisted groundcrew having higher levels than enlisted flyers. Consequently, adjustment for military occupation in statistical models using dioxin as a measure of exposure may improperly mask an actual dioxin effect. However, occupation also can be a surrogate for socioeconomic effects. Failure to adjust for occupation could overlook important risk factors related to lifestyle. If occupation was found to be significantly associated with a dependent variable in the 1992 followup analyses and was retained in the final statistical models using dioxin as a measure of exposure, the dioxin effect was evaluated in the context of two models. Analyses were performed with and without occupation in the final models to investigate whether conclusions regarding the association between the health endpoint and dioxin differed.

Similarly, body fat exhibited a significant positive association with dioxin in the serum dioxin analysis of the 1987 followup data. Body fat also was found to be significantly associated with dioxin in the 1992 followup analyses, as discussed in Chapter 9, General Health. Consequently, clinical endpoints in the Pulmonary Assessment may be related to dioxin due to the association between dioxin and body fat. To investigate this possibility, the dioxin effect was evaluated in the context of two models whenever body fat was retained in the final model. Analyses again were performed with and without body fat in the model to investigate whether conclusions regarding the association between the health endpoint and dioxin differed.

The results of the analyses without occupation and body fat in the final adjusted model are presented in Appendix P-3 and are discussed in the text only if the level of significance differs from the original final adjusted model (significant versus nonsignificant).

Longitudinal Analysis

Longitudinal analyses were performed to evaluate associations between exposure and the change in the ratio of observed FEV_1 to observed FVC between the 1982 Baseline examination and the 1992 followup. Chapter 7, Statistical Methods, contains a further discussion of methods used in the longitudinal analysis.

Table 20-1.
Statistical Analyses for the Pulmonary Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Candidate Covariates	Statistical Analysis
Asthma	MR-V	D	Yes No	AGE,RACE,OCC, PACKYR,BFAT,IC	U:LR,CS A:LR
Bronchitis	MR-V	D	Yes No	AGE,RACE,OCC, PACKYR,BFAT,IC	U:LR,CS A:LR
Pneumonia	MR-V	D	Yes No	AGE,RACE,OCC, PACKYR,BFAT,IC	U:LR,CS A:LR
Thorax and Lung Abnormalities	PE	D	Yes No	AGE,RACE,OCC, CSMOK,PACKYR, BFAT,IC	U:LR,CS A:LR
X Ray Interpretation	LAB	D	Abnormal Normal	AGE,RACE,OCC, CSMOK,PACKYR, BFAT,IC	U:LR,CS A:LR
Forced Vital Capacity (FVC) (percent of predicted)	LAB	C	--	AGE,RACE,OCC, CSMOK,PACKYR, BFAT,IC	U:GLM,TT A:GLM
Forced Expiratory Volume in 1 Second (FEV_1) (percent of predicted)	LAB	C	--	AGE,RACE,OCC, CSMOK,PACKYR, BFAT,IC	U:GLM,TT A:GLM
Ratio of Observed FEV_1 to Observed FVC	LAB	C	--	AGE,RACE,OCC, CSMOK,PACKYR, BFAT,IC	U:GLM,TT A:GLM L:GLM
Loss of Vital Capacity	LAB	D	Moderate or Severe Mild None	AGE,RACE,OCC, CSMOK,PACKYR, BFAT,IC	U:PR,CS A:PR
Obstructive Abnormality	LAB	D	Moderate or Severe Mild None	AGE,RACE,OCC, CSMOK,PACKYR, BFAT,IC	U:PR,CS A:PR

Table 20-1. (Continued)
Statistical Analyses for the Pulmonary Assessment

Covariates

Variable (Abbreviation)	Data Source	Data Form	Cutpoints
Age (AGE)	MIL	D/C	Born $\geq$ 1942 Born $<$ 1942
Race (RACE)	MIL	D	Black Non-Black
Occupation (OCC)	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Current Cigarette Smoking (CSMOK) (cigarettes/day)	Q-SR	D/C	0-Never 0-Former $>$0-20 $>$20
Lifetime Cigarette Smoking History (PACKYR) (pack-years)	Q-SR	D/C	0 $>$0-10 $>$10
Body Fat (BFAT) (percent)	PE	D/C	Lean or Normal: $\leq$25% Obese: $>$25%
Industrial Chemicals Exposure (IC)	Q-SR	D	Yes No

Abbreviations

Data Source:
- LAB = 1992 laboratory results
- MIL = Air Force military records
- MR-V = Medical records (verified)
- PE = 1992 physical examination
- Q-SR = Health questionnaires (self-reported)

Data Form:
- C = Continuous analysis only
- D = Discrete analysis only
- D/C = Appropriate form for analysis (either discrete or continuous)

Statistical Analyses:
- U = Unadjusted analyses
- A = Adjusted analyses
- L = Longitudinal analyses

Statistical Methods:
- CS = Chi-square contingency table analysis (continuity-adjusted for 2 $\times$ 2 tables)
- GLM = General linear models analysis
- LR = Logistic regression analysis
- PR = Polytomous logistic regression analysis
- TT = Two-sample t-test

Table 20-2.
Number of Participants with Missing Data for, or Excluded from, the Pulmonary Assessment

Variable	Variable Use	Group		Dioxin (Ranch Hands Only)		Categorized Dioxin	
		Ranch Hand	Comparison	Initial	Current	Ranch Hand	Comparison
X Ray Interpretation	DEP	1	0	1	1	1	0
FVC	DEP	1	1	0	1	1	1
FEV_1	DEP	1	1	0	1	1	1
Ratio of Observed FEV_1 to Observed FVC	DEP	1	1	0	1	1	1
Loss of Vital Capacity	DEP	1	1	0	1	1	1
Obstructive Abnormality	DEP	1	1	0	1	1	1
Current Cigarette Smoking	COV	0	2	0	0	0	2
Lifetime Cigarette Smoking History	COV	1	2	0	1	1	2
Pre-SEA Asthma	EXC	10	8	6	10	10	7
Pre-SEA Bronchitis	EXC	26	28	15	25	25	23
Pre-SEA Pneumonia	EXC	49	55	25	49	49	43

Abbreviations: DEP = Dependent variable (missing data).
COV = Covariate (missing data).
EXC = Exclusion.

Note: 952 Ranch Hands and 1,281 Comparisons;
520 Ranch Hands for initial dioxin; 894 Ranch Hands for current dioxin;
894 Ranch Hands and 1,063 Comparisons for categorized dioxin.

One Ranch Hand missing total lipids for current dioxin.

RESULTS

Dependent Variable-Covariate Associations

Results from the tests of association between the pulmonary dependent variables and covariates are presented in Appendix Table P-1-1. These associations are based on combined group data, and participants with pre-SEA duty occurrences of asthma, bronchitis, or pneumonia were excluded from the association analyses of the respective dependent variables.

A statistically significant association was found between post-SEA asthma and lifetime cigarette smoking history (p=0.049). A higher percentage of participants with 10 or fewer pack-years had a history of post-SEA asthma (4.6%), as compared to participants who never smoked (2.6%) and participants with more than 10 pack-years (2.6%).

The association between post-SEA bronchitis and lifetime cigarette smoking history also was significant (p<0.001). The percentage of participants with a history of bronchitis increased as the number of pack-years increased (0 pack-years: 13.5%, >0-10 pack-years: 16.7%, >10 pack-years: 21.4%). Bronchitis also was significantly associated with industrial chemicals exposure (p=0.026). Of participants who reported exposure to industrial chemicals, 19.4 percent had a history of post-SEA bronchitis versus 15.6 percent in participants without reported exposure.

A history of post-SEA pneumonia was found to be significantly associated with age and lifetime cigarette smoking history (p=0.010 and p=0.003 respectively). Of older participants, 12.1 percent had a history of post-SEA pneumonia versus 8.5 percent of younger participants. A history of pneumonia was more prevalent among participants with greater than 10 pack-years (13.1%) as compared to participants who never smoked (9.4%) and those with 10 or fewer pack-years (8.1%).

Statistically significant associations were found between the occurrence of thorax and lung abnormalities and age, occupation, current cigarette smoking, and lifetime cigarette smoking history (p<0.001 for each analysis). Results indicated that the prevalence of thorax and lung abnormalities increased with age, number of cigarettes per day, and number of pack-years. Within the occupation categories, the enlisted flyers exhibited the highest percentage of abnormalities (17.0%) compared to the enlisted groundcrew (13.4%) and officers (8.5%). The highest percentage of abnormalities among all strata of significant covariates occurred in participants who smoke more than 20 cigarettes per day (38.7%). Of interest, over the 10-year course of these examinations, the percentage of participants who currently smoke has steadily decreased from 42 percent in 1982 to 25 percent in 1992.

Association tests for x ray interpretation revealed significant relationships with age and lifetime cigarette smoking history (p<0.001 and p=0.009 respectively). A higher percentage of older participants (16.1%) than younger participants (10.0%) had an abnormal x ray interpretation. A direct relationship also was found with lifetime cigarette smoking history. The percentage of abnormal x ray interpretations increased with the number of pack-years (0 pack-years: 11.1%, 0-10 pack-years: 12.0%, >10 pack-years: 16.0%).

The following covariates were significantly associated with FVC (percent of predicted): age, race, occupation, current cigarette smoking, lifetime cigarette smoking history, and body fat ($p<0.001$ for all analyses). For age, current cigarette smoking, lifetime cigarette smoking history, and body fat, the association with FVC was inverse in nature such that as the covariate increased, the percent of predicted FVC decreased. The mean percent of predicted FVC was lower for Blacks (88.0) than for non-Blacks (101.1). The means also were lower for enlisted participants (flyers: 99.1, groundcrew: 99.3) than for officers (102.0). For FVC, lower values indicate greater compromise in lung function.

Associations involving FEV_1 (percent of predicted) are similar to the covariate associations involving FVC. All associations between FEV_1 and each of the continuously-scaled covariates were inverse (age: $r=-0.213$, $p<0.001$, current cigarette smoking: $r=-0.210$, $p<0.001$, lifetime cigarette smoking history: $r=-0.295$, $p<0.001$, body fat: $r=-0.048$, $p=0.024$). Non-Blacks exhibited a higher mean FEV_1, (95.5) than Blacks (86.8), and the enlisted flyer mean (91.8) was the lowest of the occupation strata ($p<0.001$ for race and occupation). For FEV_1, lower values indicated an adverse health effect in pulmonary function.

The ratio of observed FEV_1 to observed FVC displayed highly significant covariate associations with age, race, occupation, current cigarette smoking, lifetime cigarette smoking history, and body fat ($p<0.001$ for all analyses). Due to the distribution of the data, a natural logarithm (1-X) transformation was used. Because of this transformation, a negative correlation between the covariate and the transformed variable implies a positive association between the covariate and the ratio of observed FEV_1 to observed FVC and vice versa. Positive correlations were displayed between the transformed variable and age ($r=0.326$), current cigarette smoking ($r=0.192$), and lifetime cigarette smoking history ($r=0.299$). These positive correlations between the covariate and the transformed variable suggest that as the covariate increases, the ratio of FEV_1 to FVC tends to decrease. The association between body fat and the transformed variable was negative ($r=-0.182$) indicating that as body fat increases, the ratio of FEV_1 to FVC also tends to increase. The mean ratio for Blacks (0.797) was higher than for non-Blacks (0.759), and among the occupational strata, the mean ratio was higher for enlisted groundcrew (0.773) than for officers (0.754) and enlisted flyers (0.748). In general, higher values of the ratio of FEV_1 to FVC (approaching 1) are medically preferable. However, if the increase in the ratio is due primarily to the decrease in FVC (the denominator), then the increase in the ratio represents an artificial increase in pulmonary function (which appears to be the case for these data).

Statistically significant associations were found between loss of vital capacity and each of the following covariates: age ($p=0.001$), race ($p<0.001$), current cigarette smoking ($p=0.001$), lifetime cigarette smoking history ($p=0.003$), and body fat ($p=0.001$). Participants born before 1942 exhibited a higher prevalence of loss of vital capacity (mild: 7.4%, moderate or severe: 1.6%) than those born during or after 1942 (mild: 4.2%, moderate or severe: 0.6%). Black participants demonstrated a higher prevalence of loss of vital capacity (mild: 17.6%, moderate or severe: 6.1%) than non-Black participants (mild: 5.3%, moderate or severe: 0.9%). Results also indicate that the prevalence of mild and moderate or severe loss of vital capacity increases as the number of cigarettes per day and number of pack-years increase. Participants in the obese body fat category exhibited higher prevalences of both mild (8.4%) and moderate or severe (2.1%) losses of vital capacity than participants in the normal or lean category (mild: 5.2%, moderate or severe: 0.9%).

When tested for association, obstructive abnormality was found to be significantly associated with age ($p<0.001$), occupation ($p<0.001$), current and lifetime cigarette smoking ($p<0.001$), and body fat ($p=0.023$). The prevalence of obstructive abnormalities was higher for older participants (mild: 45.6, moderate or severe: 10.3) than for younger participants (mild: 23.8, moderate or severe: 2.7). The enlisted flyers exhibited a higher prevalence of both mild and moderate or severe obstructive abnormalities than the officers and the enlisted groundcrew. Percentages of obstructive abnormalities also increased as the number of cigarettes smoked each day increased and as the number of pack-years increased. The prevalence of obstructive abnormalities was higher for participants with lean or normal body fat (mild: 37.3%, moderate or severe: 7.6%) than for participants in the obese body fat category (mild: 33.2%, moderate or severe: 5.5%).

Exposure Analysis

The following section presents results of the statistical analyses of the dependent variables shown in Table 20-1. Dependent variables are grouped into three sections: those derived and verified from a review of medical records, data obtained during the 1992 physical examination, and data derived from the laboratory portion of the 1992 followup examination.

Unadjusted and adjusted analyses of six models are presented for each variable. Model 1 examines the relationship between the dependent variable and group (Ranch Hand or Comparison). Model 2 explores the relationship between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin level greater than 10 ppt. If a participant did not have a 1987 dioxin level, a 1992 level was used. A statistical adjustment for the percent of body fat at the participant's time of duty in SEA and the change in the percent body fat from the time of duty in SEA to the date of the blood draw for dioxin is included in this model to account for body-fat-related differences in elimination rate (31). Model 3 dichotomizes the Ranch Hands in Model 2 based on their initial dioxin measures; these two categories of Ranch Hands are referred to as the "low Ranch Hand" category and the "high Ranch Hand" category. These participants are added to Ranch Hands and Comparisons with current serum dioxin levels (1987, if available; 1992, if the 1987 level was not available) at or below 10 ppt to create a total of four categories. Ranch Hands with current serum dioxin levels at or below 10 ppt are referred to as the "background Ranch Hand" category. The relationship between the dependent variable in each of the three Ranch Hand categories and the dependent variable in the "Comparison" category is examined. A fourth contrast, exploring the relationship of the dependent variable in the low Ranch Hand category and the high Ranch Hand category combined, also is conducted. This combination is referred to in the text and tables as the "low plus high Ranch Hand" category. As in Model 2, a statistical adjustment is made for percent body fat at the participant's time of duty in SEA and the change in the percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

Models 4, 5, and 6 examine the relationship between the dependent variable and 1987 dioxin levels in all Ranch Hands with a dioxin measurement. If a participant did not have a 1987 dioxin measurement, a 1992 measurement was utilized in determining the current dioxin level. The measure of dioxin in Model 4 is lipid-adjusted, whereas whole-weight dioxin is used in Models 5 and 6. Model 6 differs from Model 5 in that a statistical adjustment for total lipids is included in Model 6. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7 respectively.

Results of investigations for group-by-covariate and dioxin-by-covariate interactions are referenced in the text, and tabular results are presented in Appendix P-2. As described previously, additional analyses were performed when occupation or body fat was retained in the final model for Models 2 through 6. Results excluding occupation and body fat from these models are tabled in Appendix P-3, and dioxin-by-covariate interactions with occupation and body fat excluded from these models are presented in Appendix P-4. Results from analyses excluding occupation and body fat are discussed in the text only if a meaningful change in the results occurred (that is, changes between significant results, marginally significant results, and nonsignificant results).

Verified Medical Records Variables

Asthma

The Model 1 unadjusted and adjusted analyses of post-SEA asthma exhibited no significant associations between group and post-SEA asthma (Table 20-3(a,b): $p>0.12$ for all contrasts). The final adjusted model included significant occupation-by-body fat and age-by-body fat interactions.

Similar to the results for Model 1, the analysis of post-SEA asthma within Models 2 and 3 found no significant results (Table 20-3(c-f): $p\geq0.15$ for all analyses). The final adjusted model for Model 2 included the significant interactions of age-by-lifetime cigarette smoking history and race-by-body fat. The interactions of age-by-race, race-by-lifetime cigarette smoking history, race-by-body fat, and occupation-by-body fat were significant in the Model 3 final adjusted model.

Current dioxin levels were examined for a significant relationship with post-SEA asthma in Models 4, 5, and 6. All unadjusted analysis results were nonsignificant (Table 20-3(g): $p>0.61$ for all analyses). Adjusted analyses of Models 4 and 6 revealed a significant current dioxin-by-age interaction (Table 20-3(h): $p=0.049$ and $p=0.037$ respectively). Results stratified by age categories are presented in Appendix Table P-2-1. Results for Models 4 and 6 reported in Table 20-3(h) were derived from the final model after deletion of the current dioxin-by-age interaction. No significant associations between the history of asthma and current dioxin were uncovered from the adjusted analyses of Models 4, 5, and 6 (Table 20-3(h): $p>0.67$ for all contrasts). The interactions of age-by-race and race-by-body fat were significant for Models 4, 5, and 6; occupation-by-body fat was also significant in Model 4, and occupation was significant in Model 5.

Table 20-3.
Analysis of Asthma

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***942***	***3.9***	***1.49 (0.93,2.39)***	***0.124***
	Comparison	***1,273***	***2.7***		
Officer	Ranch Hand	364	4.4	1.72 (0.82,3.63)	0.209
	Comparison	500	2.6		
Enlisted Flyer	Ranch Hand	160	1.9	0.95 (0.21,4.29)	0.999
	Comparison	202	2.0		
Enlisted Groundcrew	Ranch Hand	418	4.3	1.47 (0.75,2.88)	0.346
	Comparison	571	3.0		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.44 (0.89,2.32)***	***0.139***	AGE*BFAT (p=0.048)
Officer	1.73 (0.82,3.64)	0.149	OCC*BFAT (p=0.002)
Enlisted Flyer	0.61 (0.11,3.36)	0.574	
Enlisted Groundcrew	1.42 (0.72,2.79)	0.310	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 20-3. (Continued)
Analysis of Asthma

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log_2 (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	171	4.7	1.17 (0.84,1.62)	0.357
Medium	172	1.7		
High	171	5.3		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
514	1.11 (0.77,1.62)	0.573	AGE*PACKYR (p=0.027) RACE*BFAT (p=0.010)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 20-3. (Continued)
Analysis of Asthma

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,056	2.7		
Background RH	370	4.3	1.59 (0.85,2.97)	0.150
Low RH	257	3.9	1.46 (0.70,3.04)	0.314
High RH	257	3.9	1.43 (0.69,3.00)	0.336
Low plus High RH	514	3.9	1.45 (0.81,2.59)	0.215

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,054			AGE*RACE (p=0.025) RACE*PACKYR (p=0.017) RACE*BFAT (p=0.014) OCC*BFAT (p=0.011)
Background RH	369	1.48 (0.77,2.84)	0.237	
Low RH	257	1.29 (0.58,2.85)	0.534	
High RH	257	1.28 (0.58,2.82)	0.547	
Low plus High RH	514	1.28 (0.69,2.38)	0.431	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 20-3. (Continued)
Analysis of Asthma

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	3.4 (292)	4.7 (296)	4.1 (296)	1.05 (0.84,1.32)	0.653
5	4.7 (297)	3.1 (293)	4.4 (294)	1.00 (0.82,1.21)	0.973
6[c]	4.7 (296)	3.1 (293)	4.4 (294)	1.06 (0.85,1.30)	0.619

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	884	1.06 (0.80,1.42)**	0.674**	CURR*AGE (p=0.049) AGE*RACE (p=0.010) RACE*BFAT (p=0.007) OCC*BFAT (p=0.036)
5	884	0.99 (0.78,1.27)	0.962	AGE*RACE (p=0.010) RACE*BFAT (p=0.006) OCC (p=0.037)
6[d]	883	1.01 (0.80,1.27)**	0.965**	CURR*AGE (p=0.037) AGE*RACE (p=0.008) RACE*BFAT (p=0.004)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of the interaction; refer to Appendix Table P-2-1 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.
CURR = Log_2 (current dioxin + 1).

Bronchitis

Differences between Ranch Hands and Comparisons were marginally significant in the Model 1 unadjusted and adjusted analyses of post-SEA bronchitis (Table 20-4(a,b): $p=0.098$, Est. $RR=1.21$; and $p=0.092$, Adj. $RR=1.21$ respectively). The percentage of Ranch Hands with a history of bronchitis (19.4%) was greater than the corresponding percentage of Comparisons (16.6%). When group differences were examined within occupation categories, enlisted flyers exhibited significant results in both the unadjusted and adjusted analyses (Table 20-4(a,b): $p=0.037$, Est. $RR=1.78$; and $p=0.033$, Adj. $RR=1.75$ respectively). A significantly higher percentage of Ranch Hand enlisted flyers had a history of bronchitis (26.9%) than the Comparison enlisted flyers (17.2%). No significant differences were found within the officer and enlisted groundcrew categories (Table 20-4(a,b): $p>0.23$ for all remaining contrasts). The covariates and interactions in the adjusted final model were industrial chemicals exposure, an occupation-by-body fat interaction, and an age-by-lifetime cigarette smoking history interaction.

None of the unadjusted analyses for Models 2 and 3 exhibited a significant association between post-SEA bronchitis and initial dioxin (Table 20-4(c,e): $p>0.11$ for all analyses). No significant covariates were retained in the Model 2 final adjusted model. In the Model 3 adjusted analyses, a significantly higher percentage of background Ranch Hands had a history of bronchitis (21.4%) than Comparisons (17.5%) (Table 20-4(f): $p=0.036$, Adj. $RR=1.40$). When occupation and body fat were removed from the final model, the results became marginally significant (Appendix Table P-3-2: $p=0.065$, Adj. $RR=1.33$). All other Model 3 adjusted contrasts were nonsignificant (Table 20-4(f): $p>0.84$ for all remaining contrasts). Significant covariates for Model 3 included lifetime cigarette smoking history, industrial chemicals exposure, and the interaction of occupation-by-body fat.

The unadjusted analyses for Models 4 and 5 uncovered no significant relationship between post-SEA bronchitis and current dioxin (Table 20-4(g): $p>0.14$ for both analyses). The unadjusted analysis of Model 6 displayed a marginally significant inverse association between current dioxin and post-SEA bronchitis (Table 20-4(g): $p=0.089$). The adjusted analysis of each model displayed a significant current dioxin-by-industrial chemical exposure interaction. Stratified results for each level of the interaction are presented in Appendix Table P-2-2. The final adjusted models, presented after deletion of the interaction, each indicate a significant inverse association between bronchitis and current dioxin (Table 20-4(h): $p\leq0.031$, Adj. $RR\leq0.89$ for all analyses). Occupation was a significant covariate in Models 4, 5, and 6, and lifetime cigarette smoking history also was included in Models 4 and 5. When occupation was removed from the final models, the results for Model 4 became marginally significant (Appendix Table P-3-2: $p=0.076$, Adj. $RR=0.90$), and the results for Model 5 became nonsignificant ($p=0.138$).

Pneumonia

In the unadjusted analysis of Model 1, the percentage of Ranch Hands with a history of pneumonia (8.5%) was significantly lower than the corresponding percentage of Comparisons (12.0%) (Table 20-5(a): $p=0.012$, Est. $RR=0.68$). Group contrasts evaluated within each occupation category exhibited similar results for the officer category (Table 20-5(a): Ranch

Table 20-4.
Analysis of Bronchitis

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***926***	***19.4***	***1.21 (0.97,1.51)***	***0.098***
	Comparison	***1,253***	***16.6***		
Officer	Ranch Hand	354	15.8	1.00 (0.68,1.45)	0.999
	Comparison	491	15.9		
Enlisted Flyer	Ranch Hand	156	26.9	1.78 (1.07,2.96)	0.037
	Comparison	198	17.2		
Enlisted Groundcrew	Ranch Hand	416	19.7	1.20 (0.86,1.66)	0.319
	Comparison	564	17.0		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.21 (0.97,1.51)***	***0.092***	IC (p=0.066) OCC*BFAT (p=0.006) AGE*PACKYR (p=0.031)
Officer	0.99 (0.68,1.44)	0.943	
Enlisted Flyer	1.75 (1.05,2.93)	0.033	
Enlisted Groundcrew	1.22 (0.88,1.70)	0.237	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 20-4. (Continued)
Analysis of Bronchitis

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			**Analysis Results for Log₂ (Initial Dioxin)[a]**	
Initial Dioxin	**n**	**Percent Yes**	**Estimated Relative Risk (95% C.I.)[b]**	**p-Value**
Low	165	17.6	1.00 (0.84,1.19)	0.979
Medium	172	18.6		
High	168	17.3		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[a]			
n	**Adj. Relative Risk (95% C.I.)[b]**	**p-Value**	**Covariate Remarks**
505	1.00 (0.84,1.19)	0.979	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 20-4. (Continued)
Analysis of Bronchitis

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,040	17.5		
Background RH	364	21.4	1.27 (0.94,1.72)	0.116
Low RH	251	17.9	1.04 (0.72,1.49)	0.847
High RH	254	17.7	1.02 (0.71,1.47)	0.902
Low plus High RH	505	17.8	1.03 (0.78,1.36)	0.838

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,038			PACKYR (p=0.027) IC (p=0.050) OCC*BFAT (p=0.002)
Background RH	363	1.40 (1.02,1.91)	0.036	
Low RH	251	0.98 (0.68,1.41)	0.917	
High RH	254	0.96 (0.66,1.40)	0.841	
Low plus High RH	505	0.97 (0.73,1.29)	0.844	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 20-4. (Continued)
Analysis of Bronchitis

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	20.9 (287)	18.7 (289)	18.4 (293)	0.92 (0.81,1.03)	0.143
5	22.2 (293)	17.9 (285)	17.9 (291)	0.94 (0.85,1.04)	0.238
6[c]	21.9 (292)	17.9 (285)	17.9 (291)	0.91 (0.82,1.01)	0.089

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	868	0.84 (0.74,0.96)**	0.011**	CURR*IC (p=0.029) OCC (p=0.022) PACKYR (p=0.119)
5	868	0.89 (0.79,0.99)**	0.031**	CURR*IC (p=0.020) OCC (p=0.036) PACKYR (p=0.107)
6[d]	868	0.84 (0.74,0.94)**	0.004**	CURR*IC (p=0.020) OCC (p=0.014)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from model after deletion of this interaction; refer to Appendix Table P-2-2 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 20-5.
Analysis of Pneumonia

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***903***	***8.5***	***0.68 (0.51,0.92)***	***0.012***
	Comparison	***1,226***	***12.0***		
Officer	Ranch Hand	346	8.4	0.59 (0.37,0.93)	0.029
	Comparison	473	13.5		
Enlisted Flyer	Ranch Hand	151	11.3	1.00 (0.51,1.95)	0.999
	Comparison	195	11.3		
Enlisted Groundcrew	Ranch Hand	406	7.6	0.67 (0.43,1.06)	0.108
	Comparison	558	10.9		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.68 (0.51,0.91)***	***0.008***	RACE (p=0.070) BFAT (p=0.071) AGE*PACKYR (p=0.032)
Officer	0.57 (0.36,0.90)	0.017	
Enlisted Flyer	0.99 (0.50,1.94)	0.965	
Enlisted Groundcrew	0.68 (0.43,1.07)	0.096	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 20-5. (Continued)
Analysis of Pneumonia

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	160	9.4	0.87 (0.67,1.14)	0.309
Medium	168	6.0		
High	167	7.2		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[a]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
495	0.87 (0.67,1.14)	0.309	

[a] Adjusted for percent body fat at the time of duty in SEA, and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 20-5. (Continued)
Analysis of Pneumonia

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,020	12.5		
Background RH	350	10.6	0.85 (0.58,1.26)	0.424
Low RH	243	8.2	0.62 (0.38,1.01)	0.055
High RH	252	6.7	0.49 (0.29,0.83)	0.008
Low plus High RH	495	7.5	0.55 (0.37,0.81)	0.002

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,018			BFAT (p=0.098) AGE*PACKYR (p=0.029)
Background RH	349	0.85 (0.57,1.26)	0.421	
Low RH	243	0.59 (0.36,0.97)	0.038	
High RH	252	0.50 (0.29,0.86)	0.012	
Low plus High RH	495	0.55 (0.37,0.81)	0.002	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA, and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 20-5. (Continued)
Analysis of Pneumonia

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	10.3 (273)	10.2 (283)	5.9 (289)	0.87 (0.73,1.03)	0.104
5	11.9 (278)	8.2 (281)	6.3 (286)	0.90 (0.78,1.04)	0.145
6[c]	11.9 (277)	8.2 (281)	6.3 (286)	0.89 (0.77,1.04)	0.156

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	844	0.86 (0.72,1.03)	0.095	AGE*PACKYR (p=0.009)
5	844	0.89 (0.77,1.03)	0.127	AGE*PACKYR (p=0.009)
6[d]	843	0.90 (0.76,1.05)	0.173	AGE*PACKYR (p=0.008)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Hands: 8.4%, Comparisons: 13.5%, p=0.029, Est. RR=0.59). Adjusted results also indicated a significant overall and officer group difference (Table 20-5(b): p=0.008, Adj. RR=0.68 and p=0.017, Adj. RR=0.57 respectively), and a marginally significant difference was found between Ranch Hands and Comparisons within the enlisted groundcrew stratum (Table 20-5(b): p=0.096, Adj. RR=0.68). In each of these analyses, more Comparisons had a history of post-SEA pneumonia than did Ranch Hands. An age-by-lifetime cigarette smoking history interaction, race, and body fat were retained in the final model.

The results of the Model 2 unadjusted analysis of post-SEA pneumonia were nonsignificant (Table 20-5(c): p=0.309, Est. RR=0.87). No covariates were significant in the adjusted model; thus, the unadjusted and adjusted results are identical. However, the Model 3 initial dioxin unadjusted and adjusted analyses detected several significant relationships. The contrast between Comparisons and Ranch Hands in the low initial dioxin category was marginally significant for the unadjusted analysis and significant for the adjusted analysis (Table 20-5(e,f): p=0.055, Est. RR=0.62 and p=0.038, Adj. RR=0.59 respectively). Fewer Ranch Hands in the low initial dioxin category had a history of pneumonia (8.2%) than the Comparisons (12.5%). The contrasts involving participants in the high Ranch Hand and low plus high Ranch Hand categories similarly demonstrated a significantly lower percentage of Ranch Hands with a history of post-SEA pneumonia than Comparisons (Table 20-5(e,f): p≤0.012 and Est. RR ≤0.55 for each contrast). Body fat and an age-by-lifetime cigarette smoking history interaction were retained in the Model 3 adjusted analysis.

For the unadjusted and adjusted analyses of post-SEA pneumonia for Models 4, 5, and 6, the adjusted analysis of Model 4 revealed a marginally significant negative association between history of pneumonia and current dioxin (Table 20-5(h): p=0.095, Adj. RR=0.86). All other analyses exhibited nonsignificant relationships between current dioxin and the occurrence of pneumonia (Table 20-5(g,h): p>0.10 for all analyses). The interaction of age-by-lifetime cigarette smoking history was significant in the final adjusted Models 4, 5, and 6.

Physical Examination Variable

Thorax and Lung Abnormalities

In the unadjusted and adjusted analyses of Model 1, significant differences between Ranch Hands and Comparisons in the occurrence of thorax and lung abnormalities were found overall and for the enlisted flyers specifically (Table 20-6(a): p=0.011, Est. RR=1.40 and p=0.012, Est. RR=2.11 respectively; Table 20-6(b): p=0.033, Est. RR=1.36 and p=0.021, Est. RR=2.07). For the overall category, the percentages of thorax and lung abnormalities were higher for Ranch Hands (14.2%) than for Comparisons (10.5%). Similarly, for enlisted flyers, the percentages were 22.8 for Ranch Hands and 12.3 for Comparisons. Significant covariates in the adjusted analysis of thorax and lung abnormalities included an age-by-lifetime cigarette smoking history interaction, occupation, and current cigarette smoking.

Model 2 unadjusted and adjusted analyses found no significant relationship between initial dioxin and thorax and lung abnormalities (Table 20-6(c,d): p>0.28 for all analyses).

Table 20-6.
Analysis of Thorax and Lung Abnormalities

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***952***	***14.2***	***1.40 (1.09,1.81)***	***0.011***
	Comparison	***1,281***	***10.5***		
Officer	Ranch Hand	367	10.1	1.41 (0.88,2.27)	0.197
	Comparison	502	7.4		
Enlisted Flyer	Ranch Hand	162	22.8	2.11 (1.21,3.68)	0.012
	Comparison	203	12.3		
Enlisted Groundcrew	Ranch Hand	423	14.4	1.16 (0.81,1.67)	0.480
	Comparison	576	12.7		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***1.36 (1.03,1.81)***	***0.033***	OCC (p<0.001) CSMOK (p<0.001) AGE*PACKYR (p=0.027)
Officer	1.40 (0.83,2.36)	0.206	
Enlisted Flyer	2.07 (1.12,3.82)	0.021	
Enlisted Groundcrew	1.11 (0.74,1.67)	0.602	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 20-6. (Continued)
Analysis of Thorax and Lung Abnormalities

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Yes	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	174	10.3	1.11 (0.92,1.35)	0.284
Medium	173	15.6		
High	173	12.7		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
520	1.11 (0.87,1.42)	0.399	AGE ($p<0.001$) OCC ($p=0.027$) CSMOK ($p<0.001$) PACKYR ($p=0.109$)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 20-6. (Continued)
Analysis of Thorax and Lung Abnormalities

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Yes**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,063	10.4		
Background RH	374	15.2	1.48 (1.04,2.09)	0.028
Low RH	260	11.9	1.14 (0.74,1.75)	0.547
High RH	260	13.8	1.44 (0.96,2.17)	0.078
Low plus High RH	520	12.9	1.29 (0.93,1.78)	0.133

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,061			AGE ($p<0.001$) OCC ($p=0.001$) CSMOK ($p<0.001$) PACKYR ($p=0.003$)
Background RH	373	1.68 (1.12,2.50)	0.011	
Low RH	260	1.10 (0.69,1.75)	0.683	
High RH	260	1.26 (0.80,1.99)	0.316	
Low plus High RH	520	1.18 (0.82,1.69)	0.368	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 20-6. (Continued)
Analysis of Thorax and Lung Abnormalities

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Yes/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	16.3 (295)	11.3 (300)	14.1 (299)	0.94 (0.82,1.07)	0.334
5	15.3 (300)	12.5 (297)	13.8 (297)	0.95 (0.85,1.07)	0.408
6[c]	15.1 (299)	12.5 (297)	13.8 (297)	0.94 (0.84,1.06)	0.339

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	893	0.93 (0.79,1.09)**	0.369**	CURR*CSMOK (p=0.039) AGE (p<0.001) PACKYR (p=0.108) OCC*CSMOK (p=0.010)
5	893	0.95 (0.83,1.08)	0.446	AGE (p<0.001) PACKYR (p=0.057) OCC*CSMOK (p=0.042)
6[d]	892	0.97 (0.83,1.12)	0.665	AGE (p<0.001) PACKYR (p=0.054) OCC*CSMOK (p=0.039)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin +1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model after deletion of this interaction; refer to Appendix Table P-2-3 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Significant differences between background Ranch Hands and Comparisons in the occurrence of thorax and lung abnormalities were uncovered in the Model 3 unadjusted and adjusted analysis (Table 20-6(e,f): p=0.028, Est. RR=1.48 and p=0.011, Adj. RR=1.68 respectively). The background Ranch Hands exhibited a higher percentage of thorax and lung abnormalities (15.2%) than Comparisons (10.4%). The unadjusted analysis also revealed a marginally significant difference between participants in the high Ranch Hand category, and Comparisons (Table 20-6(e): p=0.078, Est. RR=1.44). Both Models 2 and 3 were adjusted for age, occupation, current cigarette smoking, and lifetime cigarette smoking history.

When occupation was removed from the final adjusted analysis for Model 2, the results became marginally significant (Appendix Table P-3-4: p=0.087, Adj. RR=1.22). The significant result found in the Model 3 adjusted analysis of background Ranch Hands versus Comparisons became marginally significant (p=0.059). Also, the contrast of Ranch Hands in the high dioxin category versus Comparisons was marginally significant (p=0.068, Adj. RR=1.52) when occupation was removed from Model 3.

The association between current dioxin and thorax and lung abnormalities was nonsignificant in the analyses of Models 4, 5, and 6 (Table 20-6(g,h): p>0.33 for all analyses). Each of the three final adjusted models included age, lifetime cigarette smoking history, and an occupation-by-current cigarette smoking interaction. Model 4 also had a significant current dioxin-by-current cigarette smoking interaction (p=0.039). Results stratified by each level of the interaction are presented in Appendix Table P-2-3. Adjusted results in Table 20-6 for Model 4 were derived from the final model after deletion of the current dioxin-by-current cigarette smoking interaction.

Laboratory Examination Variables

X Ray Interpretation

Results from the Model 1 analysis of x ray interpretation exhibited no significant differences between Ranch Hands and Comparisons for the overall analysis or within any of the occupation strata (Table 20-7(a,b): p>0.27 for all contrasts). Age, occupation, and a lifetime cigarette smoking history-by-body fat interaction were retained in the final model.

No significant relationship between initial dioxin and x ray interpretation was detected in the analyses of Models 2 and 3 (Table 20-7(c-f): p>0.16 for all analyses). Model 2 was adjusted for age, occupation, and current cigarette smoking. Model 3 exhibited a significant categorized dioxin-by-occupation interaction (p=0.011). Results stratified by each level of occupation are presented in Appendix Table P-2-4. Model 3 was also adjusted for age and body fat.

Similar to Models 1 through 3, all unadjusted results for Models 4 through 6 for x ray interpretation were nonsignificant (Table 20-7(g): p>0.19 for all models). When adjusted for significant covariates, the final models for 4, 5, and 6 each included a current dioxin-by-current cigarette smoking interaction (Table 20-7(h): p=0.009, p=0.031, p=0.021 respectively). Stratified results for each model are presented in Appendix Table P-2-4.

Table 20-7.
Analysis of X Ray Interpretation

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	**Group**	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***951***	***13.5***	***1.00 (0.78,1.28)***	***0.999***
	Comparison	***1,281***	***13.4***		
Officer	Ranch Hand	367	12.3	0.97 (0.65,1.47)	0.982
	Comparison	502	12.6		
Enlisted Flyer	Ranch Hand	162	19.1	1.42 (0.82,2.47)	0.271
	Comparison	203	14.3		
Enlisted Groundcrew	Ranch Hand	422	12.3	0.87 (0.60,1.27)	0.531
	Comparison	576	13.9		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED			
Occupational Category	**Adj. Relative Risk (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***0.98 (0.76,1.25)***	***0.861***	AGE (p<0.001) OCC (p=0.018) PACKYR*BFAT (p=0.030)
Officer	0.96 (0.64,1.45)	0.846	
Enlisted Flyer	1.34 (0.77,2.35)	0.302	
Enlisted Groundcrew	0.86 (0.59,1.25)	0.432	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 20-7. (Continued)
Analysis of X Ray Interpretation

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED				
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]	
Initial Dioxin	n	Percent Abnormal	Estimated Relative Risk (95% C.I.)[b]	p-Value
Low	174	10.9	0.93 (0.76,1.14)	0.490
Medium	173	16.8		
High	172	9.9		

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED			
Analysis Results for Log_2 (Initial Dioxin)[c]			
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
519	0.85 (0.67,1.07)	0.162	AGE (p=0.028) OCC (p=0.001) CSMOK (p=0.052)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 20-7. (Continued)
Analysis of X Ray Interpretation

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED				
Dioxin Category	**n**	**Percent Abnormal**	**Est. Relative Risk (95% C.I.)[ab]**	**p-Value**
Comparison	1,063	13.7		
Background RH	374	14.4	1.06 (0.75,1.48)	0.756
Low RH	260	13.5	0.98 (0.66,1.45)	0.901
High RH	259	11.6	0.83 (0.54,1.26)	0.376
Low plus High RH	519	12.5	0.90 (0.66,1.23)	0.515

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED				
Dioxin Category	**n**	**Adj. Relative Risk (95% C.I.)[ac]**	**p-Value**	**Covariate Remarks**
Comparison	1,063			DXCAT*OCC (p=0.011) AGE (p<0.001) BFAT (p=0.111)
Background RH	374	1.12 (0.79,1.59)**	0.530**	
Low RH	260	0.92 (0.62,1.38)**	0.690**	
High RH	259	0.79 (0.51,1.21)**	0.279**	
Low plus High RH	519	0.86 (0.62,1.18)**	0.343**	

[a] Relative risk and confidence interval relative to Comparisons.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model after deletion of this interaction; refer to Appendix Table P-2-4 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.
DXCAT = Categorized Dioxin.

Table 20-7. (Continued)
Analysis of X Ray Interpretation

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED					
	Current Dioxin Category Percent Abnormal/(n)			Analysis Results for Log_2 (Current Dioxin + 1)	
Model[a]	Low	Medium	High	Est. Relative Risk (95% C.I.)[b]	p-Value
4	12.9 (295)	14.0 (300)	13.1 (298)	0.94 (0.82,1.07)	0.339
5	14.0 (300)	12.8 (297)	13.2 (296)	0.97 (0.87,1.09)	0.651
6[c]	14.0 (299)	12.8 (297)	13.2 (296)	0.92 (0.82,1.04)	0.197

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED				
	Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	892	****	****	CURR*CSMOK (p=0.009) AGE (p=0.006) OCC (p=0.035) PACKYR (p=0.108)
5	892	0.95 (0.84,1.09)**	0.478**	CURR*CSMOK (p=0.031) AGE (p=0.005) OCC (p=0.054) PACKYR (p=0.104)
6[d]	892	0.88 (0.77,1.02)**	0.085**	CURR*CSMOK (p=0.021) AGE (p=0.002) OCC (p=0.016)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

[d] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model after deletion of this interaction; refer to Appendix Table P-2-4 for further analysis of this interaction.

**** Log_2 (current dioxin + 1)-by-covariate interaction ($p \leq 0.01$); adjusted relative risk, confidence interval, and p-value not presented; refer to Appendix Table P-2-4 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 20-7(h) displays adjusted results from Models 5 and 6 after deletion of the current dioxin-by-current cigarette smoking interactions. For Model 4, the stratified analyses did not exhibit a significant association between current dioxin and an abnormal x ray interpretation except for Ranch Hands who smoked more than 20 cigarettes a day ($p=0.002$, Adj. RR=0.48). For this category, the percentage of abnormal x ray interpretations decreased as the level of current dioxin increased (low = 34.6%, medium = 10.7%, high = 2.8%). Model 6 displayed a marginally significant negative association between current dioxin and x ray interpretation after deletion of the interaction between current dioxin and current cigarette smoking (Table 20-7(h): $p=0.085$, Est. RR=0.88). Models 4 and 5 also were adjusted for age, occupation, and lifetime cigarette smoking history, and Model 6 also included age and occupation. When occupation was removed from Model 6, the results became nonsignificant (Appendix Table P-3-5: $p=0.491$).

FVC

The unadjusted and adjusted Model 1 analyses of FVC revealed no significant differences in group means across or within occupational categories (Table 20-8(a,b): $p>0.25$ for all analyses). The adjusted analysis contained occupation, current cigarette smoking, body fat, an age-by-lifetime cigarette smoking history interaction, and a race-by-lifetime cigarette smoking history interaction.

The unadjusted analysis of Model 2 did not detect a significant association between initial dioxin and FVC (Table 20-8(c): $p=0.305$). However, the Model 2 adjusted analysis revealed a significant negative association between initial dioxin and FVC (Table 20-8(d): $p=0.034$). The means decreased from 94.8 percent of predicted for the low initial dioxin category to 94.3 and 91.5 percent for the medium and high initial dioxin categories. Age, race, body fat, an occupation-by-industrial chemical exposure interaction, and a lifetime cigarette smoking history-by-industrial chemicals exposure interaction were significant in Model 2.

For the unadjusted Model 3 analysis, the contrast of Comparisons versus Ranch Hands in the low plus high dioxin category was marginally significant (Table 20-8(e): $p=0.089$). The Ranch Hands in the low plus high dioxin category had a lower mean FVC (99.2 percent) than the Comparisons (100.5 percent). All Model 3 adjusted contrasts were nonsignificant (Table 20-8(f): $p>0.18$). Current cigarette smoking, body fat, an age-by-lifetime cigarette smoking history interaction, a race-by-lifetime cigarette smoking history interaction, and an occupation-by-industrial chemicals exposure interaction were significant in Model 3. When occupation and body fat were removed from the final model, Ranch Hands in the high dioxin category had marginally significant mean lower FVC values than Comparisons (Appendix Table P-3-6: high Ranch Hands: Adj. mean=93.8 percent; Comparisons: Adj. mean=95.4 percent; $p=0.089$). For FVC, lower values indicate greater compromise in lung function.

The unadjusted analysis of FVC versus current dioxin demonstrated significant negative associations (Table 20-8(g): $p\leq 0.015$ for Models 4, 5, and 6). However, when each model was adjusted for covariate effects, all associations were nonsignificant (Table 20-8(h): $p>0.22$ for all analyses). Models 4, 5, and 6 were adjusted for age, body fat, and the interactions of lifetime cigarette smoking history-by-race, current cigarette smoking-by-

Table 20-8.
Analysis of FVC (Percent of Predicted)

a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	**Group**	**n**	**Mean**	**Difference of Means (95% C.I.)**	**p-Value**
All	***Ranch Hand***	***951***	***100.1***	***-0.3 (-1.5,0.9)***	***0.607***
	Comparison	***1,280***	***100.5***		
Officer	Ranch Hand	366	101.6	-0.8 (-2.7,1.2)	0.439
	Comparison	502	102.4		
Enlisted Flyer	Ranch Hand	162	99.8	1.3 (-1.7,4.3)	0.393
	Comparison	203	98.5		
Enlisted Groundcrew	Ranch Hand	423	99.0	-0.5 (-2.3,1.3)	0.597
	Comparison	575	99.5		

b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED						
Occupational Category	**Group**	**n**	**Adj. Mean**	**Difference of Adj. Means (95% C.I.)**	**p-Value**	**Covariate Remarks[a]**
All	***Ranch Hand***	***950***	***95.3***	***-0.2 (-1.4,0.9)***	***0.665***	OCC (p=0.027) CSMOK (p<0.001) BFAT (p<0.001) AGE*PACKYR (p=0.012) PACKYR*RACE (p=0.001)
	Comparison	***1,278***	***95.6***			
Officer	Ranch Hand	365	96.4	-0.4 (-2.2,1.4)	0.677	
	Comparison	502	96.8			
Enlisted Flyer	Ranch Hand	162	96.0	1.6 (-1.2,4.4)	0.255	
	Comparison	203	94.4			
Enlisted Groundcrew	Ranch Hand	423	94.3	-0.8 (-2.5,0.9)	0.341	
	Comparison	573	95.1			

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 20-8. (Continued)
Analysis of FVC (Percent of Predicted)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[a]		
Initial Dioxin	n	Mean	Adj. Mean[a]	R^2	Slope (Std. Error)	p-Value
Low	174	99.1	98.8	0.040	-0.471 (0.458)	0.305
Medium	173	99.8	99.7			
High	173	97.2	97.6			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[b]			
Initial Dioxin	n	Adj. Mean[b]	R^2	Adj. Slope (Std. Error)[b]	p-Value	Covariate Remarks
Low	174	94.8	0.167	-1.068 (0.502)	0.034	AGE (p=0.001) RACE (p<0.001) BFAT (p=0.007) OCC*IC (p=0.003) PACKYR*IC (p=0.015)
Medium	173	94.3				
High	173	91.5				

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 20-8. (Continued)
Analysis of FVC (Percent of Predicted)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	n	Mean	Adj. Mean[a]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,062	100.5	100.5		
Background RH	373	102.0	101.2	0.7 (-1.0,2.3)	0.439
Low RH	260	99.0	99.2	-1.3 (-3.2,0.7)	0.196
High RH	260	98.3	99.2	-1.3 (-3.2,0.6)	0.179
Low plus High RH	520	98.7	99.2	-1.3 (-2.8,0.2)	0.089

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	n	Adj. Mean[b]	Difference of Adj. Mean vs. Comparisons (95% C.I.)	p-Value	Covariate Remarks
Comparison	1,060	95.7			CSMOK ($p<0.001$) BFAT ($p<0.001$) AGE*PACKYR ($p=0.007$) PACKYR*RACE ($p<0.001$) OCC*IC ($p=0.022$)
Background RH	372	96.1	0.3 (-1.3,1.9)	0.698	
Low RH	260	95.5	-0.3 (-2.1,1.5)	0.766	
High RH	260	94.5	-1.3 (-3.1,0.6)	0.183	
Low plus High RH	520	95.0	-0.8 (-2.2,0.7)	0.298	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 20-8. (Continued)
Analysis of FVC (Percent of Predicted)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[a]	Low	Medium	High	R^2	Slope (Std. Error)	p-Value
4	102.2 (295)	99.5 (299)	98.4 (299)	0.011	-1.023 (0.323)	0.002
5	102.5 (300)	99.4 (296)	98.2 (297)	0.012	-0.919 (0.277)	0.001
6[b]	102.2 (299)	99.4 (296)	98.6 (297)	0.016	-0.728 (0.299)	0.015

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	Low	Medium	High	R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
4	95.9 (294)	95.2 (299)	94.6 (299)	0.179	-0.385 (0.360)	0.286	AGE (p<0.001) BFAT (p<0.001) PACKYR*RACE (p=0.026) CSMOK*OCC (p<0.001) OCC*IC (p=0.002) PACKYR*IC (p=0.034)
5	96.1 (299)	95.0 (296)	94.4 (297)	0.180	-0.367 (0.305)	0.228	AGE (p<0.001) BFAT (p<0.001) PACKYR*RACE (p=0.027) CSMOK*OCC (p=0.001) OCC*IC (p=0.002) PACKYR*IC (p=0.034)
6[c]	95.7 (298)	94.9 (296)	94.7 (297)	0.183	-0.172 (0.329)	0.600	AGE (p=0.001) BFAT (p<0.001) PACKYR*RACE (p=0.032) CSMOK*OCC (p=0.001) OCC*IC (p=0.002) PACKYR*IC (p=0.035)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Adjusted for log_2 total lipids.

[c] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

occupation, occupation-by-industrial chemicals exposure, and lifetime cigarette smoking history-by-industrial chemicals exposure. When occupation and body fat were removed from the final models of 4, 5, and 6, each association between current dioxin and FVC became highly significant (Appendix Table P-3-6: $p \leq 0.002$ for all models). Similar to the unadjusted analysis, the association between FVC and current dioxin was negative such that the mean FVC decreased for increasing levels of current dioxin, indicating a higher risk of lung dysfunction for higher levels of current dioxin.

FEV_1

No significant differences in means between Ranch Hands and Comparisons were revealed in the unadjusted or adjusted analysis of percent of predicted FEV_1 (Table 20-9(a,b): $p > 0.32$ for all analyses). Covariates retained in the final model were body fat, and the interactions of current cigarette smoking-by-occupation, age-by-lifetime cigarette smoking history, and race-by-lifetime cigarette smoking history.

The unadjusted Model 2 analysis and the unadjusted and adjusted Model 3 analyses did not detect any significant associations between initial dioxin and FEV_1 (Table 20-9(c,e,f): $p > 0.25$ for all analyses). The adjusted analysis for Model 2 exhibited a significant initial dioxin-by-current cigarette smoking interaction (Table 20-9(d): $p = 0.002$). Results stratified by each level of the interaction are displayed in Appendix Table P-2-5. The stratified analyses exhibited a significant negative association between initial dioxin and FEV_1 for Ranch Hands who never smoked ($p = 0.001$). The adjusted means for this stratum were 98.6, 96.4, and 90.8 percent for the low, medium, and high levels of initial dioxin respectively. The association was nonsignificant within the other current cigarette smoking strata (Appendix Table P-2-5: $p > 0.10$). The adjusted slopes of the individual smoking strata increased with a rise in the level of smoking. The final adjusted model for Model 2 also included the covariates age, race, lifetime cigarette smoking history, body fat and industrial chemicals exposure. Model 3 was adjusted for industrial chemicals exposure, and the interactions of age-by-lifetime cigarette smoking history, age-by-body fat, lifetime cigarette smoking history-by-race, current cigarette smoking-by-occupation, and body fat-by-occupation.

All analyses of Models 4, 5, and 6 resulted in nonsignificant associations between current dioxin and FEV_1 (Table 20-9(g,h): $p \geq 0.19$ for all analyses). Final adjusted models each included race, lifetime cigarette smoking history, an age-by-body fat interaction, and a current cigarette smoking-by-occupation interaction. Models 4 and 6 also included an occupation-by-industrial chemicals exposure interaction, while Model 5 also included industrial chemicals exposure.

Ratio of Observed FEV_1 to Observed FVC

Due to the distribution of the data, a natural logarithm (1-X) transformation was used. Because of this transformation, a negative slope (Models 2, 4, 5, and 6) implies a positive association between dioxin and the ratio of observed FEV_1 to observed FVC.

Table 20-9.
Analysis of FEV_1 (Percent of Predicted)

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED					
Occupational Category	Group	n	Mean	Difference of Means (95% C.I.)	p-Value
All	*Ranch Hand*	*951*	*94.6*	*-0.7 (-2.2,0.7)*	*0.329*
	Comparison	*1,280*	*95.3*		
Officer	Ranch Hand	366	95.7	-1.1 (-3.4,1.2)	0.352
	Comparison	502	96.8		
Enlisted Flyer	Ranch Hand	162	91.3	-0.9 (-4.4,2.7)	0.638
	Comparison	203	92.2		
Enlisted Groundcrew	Ranch Hand	423	94.8	-0.2 (-2.4,1.9)	0.826
	Comparison	575	95.1		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED						
Occupational Category	Group	n	Adj. Mean	Difference of Adj. Means (95% C.I.)	p-Value	Covariate Remarks[a]
All	*Ranch Hand*	*950*	*91.1*	*-0.4 (-1.7,0.9)*	*0.531*	BFAT (p<0.001)
	Comparison	*1,278*	*94.5*			CSMOK*OCC (p=0.038)
Officer	Ranch Hand	365	92.6	-0.5 (-2.6,1.6)	0.659	AGE*PACKYR (p=0.002) PACKYR*RACE (p=0.015)
	Comparison	502	93.0			
Enlisted Flyer	Ranch Hand	162	90.5	-0.1 (-3.4,3.1)	0.938	
	Comparison	203	90.6			
Enlisted Groundcrew	Ranch Hand	423	90.3	-0.5 (-2.5,1.5)	0.633	
	Comparison	573	90.8			

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 20-9. (Continued)
Analysis of FEV_1 (Percent of Predicted)

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[a]		
Initial Dioxin	n	Mean	Adj. Mean[a]	R^2	Slope (Std. Error)	p-Value
Low	174	93.9	93.9	0.006	0.125 (0.568)	0.826
Medium	173	93.7	93.7			
High	173	95.4	95.4			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[b]			
Initial Dioxin	n	Adj. Mean[b]	R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
Low	174	****	0.159	****	****	INIT*CSMOK (p=0.002) AGE (p<0.001) RACE (p<0.001) PACKYR (p<0.001) BFAT (p=0.019) IC (p=0.082)
Medium	173	****				
High	173	****				

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

**** Log_2 (initial dioxin)-by-covariate interaction ($p \leq 0.01$); adjusted mean, adjusted slope, standard error, and p-value not presented; refer to Appendix Table P-2-5 for further analysis of this interaction.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
INIT = Log_2 (initial dioxin).

Table 20-9. (Continued)
Analysis of FEV_1 (Percent of Predicted)

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	**n**	**Mean**	**Adj. Mean[a]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)**	**p-Value**
Comparison	1,062	95.3	95.3		
Background RH	373	94.7	94.6	-0.7 (-2.8,1.3)	0.492
Low RH	260	93.9	93.9	-1.4 (-3.7,1.0)	0.257
High RH	260	94.7	94.9	-0.4 (-2.8,2.0)	0.743
Low plus High RH	520	94.3	94.4	-0.9 (-2.7,0.9)	0.345

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	**n**	**Adj. Mean[b]**	**Difference of Adj. Mean vs. Comparisons (95% C.I.)**	**p-Value**	**Covariate Remarks**
Comparison	1,060	91.5			IC (p=0.066) AGE*PACKYR (p=0.003) AGE*BFAT (p=0.001) PACKYR*RACE (p=0.009) CSMOK*OCC (p=0.009) BFAT*OCC (p=0.008)
Background RH	372	90.5	-1.0 (-2.9,0.9)	0.315	
Low RH	260	91.4	-0.1 (-2.2,2.1)	0.932	
High RH	260	90.9	-0.6 (-2.8,1.6)	0.583	
Low plus High RH	520	91.2	-0.3 (-2.0,1.3)	0.684	

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 20-9. (Continued)
Analysis of FEV_1 (Percent of Predicted)

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED						
	Current Dioxin Category Mean/(n)			Analysis Results for Log_2 (Current Dioxin + 1)		
Model[a]	Low	Medium	High	R^2	Slope (Std. Error)	p-Value
4	95.0 (295)	94.0 (299)	94.4 (299)	<0.001	0.231 (0.405)	0.568
5	95.3 (300)	93.7 (296)	94.5 (297)	<0.001	0.107 (0.347)	0.757
6[b]	94.7 (299)	93.6 (296)	95.2 (297)	0.008	0.437 (0.374)	0.243

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED							
	Current Dioxin Category Adjusted Mean/(n)			Analysis Results for Log_2 (Current Dioxin + 1)			
Model[a]	Low	Medium	High	R^2	Adj. Slope (Std. Error)	p-Value	Covariate Remarks
4	89.3 (294)	90.0 (299)	90.1 (299)	0.190	0.447 (0.448)	0.318	RACE (p<0.001) PACKYR (p<0.001) AGE*BFAT (p=0.020) CSMOK*OCC (p=0.001) OCC*IC (p=0.050)
5	89.3 (299)	89.4 (296)	90.2 (297)	0.185	0.301 (0.379)	0.428	RACE (p<0.001) PACKYR (p<0.001) IC (p=0.082) AGE*BFAT (p=0.021) CSMOK*OCC (p=0.001)
6[c]	89.0 (298)	89.5 (296)	90.7 (297)	0.192	0.536 (0.409)	0.190	RACE (p<0.001) PACKYR (p<0.001) AGE*BFAT (p=0.023) CSMOK*OCC (p=0.001) OCC*IC (p=0.044)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Adjusted for log_2 total lipids.

[c] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

For the Model 1 unadjusted and adjusted analyses of the ratio of observed FEV_1 to observed FVC, all mean differences between Ranch Hands and Comparisons were nonsignificant (Table 20-10(a,b): $p>0.19$ for all contrasts). Lifetime cigarette smoking history, body fat, industrial chemical exposure, and the interactions of current cigarette smoking-by-race and age-by-occupation were included in the final model.

The Model 2 unadjusted analysis exhibited a significant inverse association between the ratio of observed FEV_1 to observed FVC and initial dioxin (Table 20-10(c): $p=0.008$). After Model 2 was adjusted for age, race, occupation, current cigarette smoking, lifetime cigarette smoking history, and industrial chemicals exposure, the association between the FEV_1 to FVC ratio and initial dioxin became nonsignificant (Table 20-10(d): $p=0.165$). Model 3 unadjusted analyses indicated significant differences in means between Comparisons and background Ranch Hands and between Comparisons and Ranch Hands in the high dioxin category (Table 20-10(e): $p=0.009$ and 0.022, Est. difference in means = -0.012 and 0.012). Adjusted contrasts revealed a marginally significant difference between Comparisons and background Ranch Hands (Table 20-10(f): $p=0.070$, Est. difference in means = -0.007). Covariates that displayed significance in Model 3 were a categorized dioxin-by-age interaction, lifetime cigarette smoking history, industrial chemicals exposure, and age-by-occupation, age-by-body fat, current cigarette smoking-by-race, and body fat-by-occupation interactions. Results in Table 20-10(f) are those from Model 3 after deletion of the categorized dioxin-by-age interaction from the final adjusted model. Stratified results for each level of age are displayed in Appendix Table P-2-6.

Analyses of Models 4 through 6 indicated significant positive associations between the ratio of observed FEV_1 to observed FVC and current dioxin (Table 20-10(g,h): $p\leq0.001$ for all analyses). For Model 4, the adjusted mean ratios were 0.767, 0.755, and 0.782 for the low, medium, and high current dioxin categories respectively; for Model 5, the adjusted mean ratios were 0.766, 0.774, 0.785, and for Model 6 the adjusted mean ratios were 0.765, 0.773, and 0.785. Due to the transformation used, the negative slope between 1 minus the FEV_1 to FVC ratio and current dioxin for each model indicates an increasing trend in the FEV_1 to FVC ratio as current dioxin increased. Each adjusted model included race, current cigarette smoking, lifetime cigarette smoking history, industrial chemicals exposure, and an age-by-body fat interaction.

Loss of Vital Capacity

The Model 1 unadjusted analysis of loss of vital capacity did not detect any overall group differences (Table 20-11(a): $p>0.26$). However, after stratifying by occupation, a marginally significant difference was detected between enlisted flyer Ranch Hands and Comparisons for the mild versus no loss of vital capacity contrast (Table 20-11(a): $p=0.089$, Est. RR=0.46). The percentage of enlisted flyer Ranch Hands with mild loss of vital capacity was lower than the percentage of Comparisons (4.3% vs. 8.9%). All other unadjusted contrasts, including those performed for moderate or severe loss versus no loss of vital capacity, were nonsignificant (Table 20-11(a): $p>0.37$ for all). Paralleling the unadjusted analysis, the adjusted analysis of mild loss versus no loss of vital capacity was also significant for the enlisted flyers (Table 20-11(b): $p=0.048$, Adj. RR=0.39). All other adjusted analyses were not significant ($p>0.24$). The Model 1 analysis was adjusted for

Table 20-10.
Analysis of Ratio of Observed FEV_1 to Observed FVC

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Mean[a]	Difference of Means (95% C.I.)[b]	p-Value[c]
All	***Ranch Hand***	***951***	***0.760***	***-0.002 --***	***0.569***
	Comparison	***1,280***	***0.762***		
Officer	Ranch Hand	366	0.752	-0.004 --	0.450
	Comparison	502	0.755		
Enlisted Flyer	Ranch Hand	162	0.741	-0.012 --	0.193
	Comparison	203	0.753		
Enlisted Groundcrew	Ranch Hand	423	0.774	0.003 --	0.496
	Comparison	575	0.771		

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Group	n	Adj. Mean[a]	Difference of Adj. Means (95% C.I.)[b]	p-Value[c]	Covariate Remarks[d]
All	***Ranch Hand***	***950***	***0.772***	***-0.001 --***	0.853	PACKYR ($p<0.001$)
	Comparison	***1,278***	***0.772***			BFAT ($p<0.001$)
Officer	Ranch Hand	365	0.770	-0.002 --	0.633	IC ($p=0.068$)
	Comparison	502	0.772			AGE*OCC ($p<0.001$)
Enlisted Flyer	Ranch Hand	162	0.768	-0.008 --	0.232	CSMOK*RACE ($p=0.003$)
	Comparison	203	0.776			
Enlisted Groundcrew	Ranch Hand	423	0.775	0.004 --	0.371	
	Comparison	573	0.772			

[a] Transformed from the natural logarithm (1-X) scale.

[b] Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm (1-X) scale.

[c] P-values based on difference of means on natural logarithm (1-X) scale.

[d] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 20-10. (Continued)
Analysis of Ratio of Observed FEV_1 to Observed FVC

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED						
Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[b]		
Initial Dioxin	n	Mean[a]	Adj. Mean[ab]	R^2	Slope (Std. Error)[c]	p-Value
Low	174	0.761	0.762	0.052	-0.029 (0.011)	0.008
Medium	173	0.758	0.759			
High	173	0.791	0.789			

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED						
Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[d]			
Initial Dioxin	n	Adj. Mean[ad]	R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
Low	174	0.781	0.201	-0.016 (0.012)	0.165	AGE (p<0.001) RACE (p=0.004) OCC (p=0.133) CSMOK (p=0.134) PACKYR (p<0.001) IC (p=0.043)
Medium	173	0.780				
High	173	0.799				

[a] Transformed from natural logarithm (1-X) scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Slope and standard error based on natural logarithm of (1 - ratio of observed FEV_1 to observed FVC) versus log_2 (initial dioxin).

[d] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 20-10. (Continued)
Analysis of Ratio of Observed FEV_1 to Observed FVC

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED					
Dioxin Category	n	Mean[a]	Adj. Mean[ab]	Difference of Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]
Comparison	1,062	0.762	0.762		
Background RH	373	0.746	0.750	-0.012 --	0.009
Low RH	260	0.763	0.762	0.000 --	0.990
High RH	260	0.778	0.774	0.012 --	0.022
Low plus High RH	520	0.770	0.768	0.006 --	0.136

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED					
Dioxin Category	n	Adj. Mean[ae]	Difference of Adj. Mean vs. Comparisons (95% C.I.)[c]	p-Value[d]	Covariate Remarks
Comparison	1,060	0.773**			DXCAT*AGE (p=0.047) PACKYR (p<0.001) IC (p=0.007) AGE*OCC (p<0.001) AGE*BFAT (p=0.006) CSMOK*RACE (p=0.018) BFAT*OCC (p=0.016)
Background RH	372	0.766**	-0.007 --**	0.070**	
Low RH	260	0.776**	0.003 --**	0.536**	
High RH	260	0.777**	0.004 --**	0.400**	
Low plus High RH	520	0.776**	0.003 --**	0.344**	

[a] Transformed from natural logarithm (1-X) scale.

[b] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[c] Difference of adjusted means after transformation to original scale; confidence interval on difference of adjusted means not presented because analysis was performed on natural logarithm (1-X) scale.

[d] P-value is based on difference of means on natural logarithm (1-X) scale.

[e] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted mean, difference of adjusted means, and p-value derived from a model after deletion of this interaction; refer to Appendix Table P-2-6 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 20-10. (Continued)
Analysis of Ratio of Observed FEV_1 to Observed FVC

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED

Model[b]	Current Dioxin Category Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Slope (Std. Error)[c]	p-Value
4	0.746 (295)	0.758 (299)	0.776 (299)	0.041	-0.046 (0.007)	<0.001
5	0.746 (300)	0.757 (296)	0.778 (297)	0.035	-0.037 (0.006)	<0.001
6[d]	0.743 (299)	0.757 (296)	0.780 (297)	0.042	-0.043 (0.007)	<0.001

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED

Model[b]	Current Dioxin Category Adjusted Mean[a]/(n) Low	Medium	High	Analysis Results for Log_2 (Current Dioxin + 1) R^2	Adj. Slope (Std. Error)[c]	p-Value	Covariate Remarks
4	0.767 (294)	0.755 (299)	0.782 (299)	0.233	-0.025 (0.007)	0.001	RACE (p=0.002) CSMOK (p=0.001) PACKYR (p<0.001) IC (p=0.014) AGE*BFAT (p=0.006)
5	0.766 (299)	0.774 (296)	0.785 (297)	0.232	-0.020 (0.006)	0.001	RACE (p=0.001) CSMOK (p=0.001) PACKYR (p<0.001) IC (p=0.016) AGE*BFAT (p=0.007)
6[e]	0.765 (298)	0.773 (296)	0.785 (297)	0.232	-0.022 (0.007)	0.001	RACE (p=0.002) CSMOK (p=0.001) PACKYR (p<0.001) IC (p=0.015) AGE*BFAT (p=0.007)

[a] Transformed from natural logarithm (1-X) scale.

[b] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for $\log_2$ total lipids.

[c] Slope and standard error based on natural logarithm of (1 - ratio of observed FEV_1 to observed FVC) versus $\log_2$ (current dioxin + 1).

[d] Adjusted for $\log_2$ total lipids.

[e] Adjusted for $\log_2$ total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 20-11.
Analysis of Loss of Vital Capacity

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED								
			Percent			Mild vs. None		Moderate or Severe vs. None	
Occupational Category	Group	n	None	Mild	Mod. or Sev.	Est. Relative Risk (95% C.I.)	p-Value	Est. Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***951***	***93.5***	***5.4***	***1.1***	***0.81 (0.57,1.17)***	***0.263***	***0.78 (0.36,1.71)***	***0.535***
	Comparison	***1,280***	***92.2***	***6.5***	***1.3***				
Officer	Ranch Hand	366	94.6	4.6	0.8	0.86 (0.46,1.60)	0.628	1.02 (0.23,4.59)	0.978
	Comparison	502	93.8	5.4	0.8				
Enlisted Flyer	Ranch Hand	162	94.5	4.3	1.2	0.46 (0.19,1.13)	0.089	0.47 (0.09,2.46)	0.371
	Comparison	203	88.6	8.9	2.5				
Enlisted Groundcrew	Ranch Hand	423	92.4	6.4	1.2	0.96 (0.58,1.60)	0.880	0.85 (0.27,2.60)	0.770
	Comparison	575	92.0	6.6	1.4				

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED					
	Mild vs. None		Moderate or Severe vs. None		
Occupational Category	Adj. Relative Risk (95% C.I.)	p-Value	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks[a]
All	***0.80 (0.55,1.16)***	***0.248***	***0.78 (0.35,1.73)***	***0.538***	AGE (p<0.001)
Officer	0.80 (0.42,1.53)	0.503	1.01 (0.22,4.60)	0.989	CSMOK (p=0.003)
Enlisted Flyer	0.39 (0.16,0.99)	0.048	0.37 (0.07,1.99)	0.244	BFAT (p<0.001) IC (p=0.114)
Enlisted Groundcrew	1.05 (0.62,1.78)	0.861	0.95 (0.30,3.02)	0.930	RACE*PACKYR (p=0.011)

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

Table 20-11. (Continued)
Analysis of Loss of Vital Capacity

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category	n	Initial Dioxin Category Summary Statistics: Percent None	Percent Mild	Percent Mod. or Sev.	Mild vs. None: Est. Relative Risk (95% C.I.)[b]	Mild vs. None: p-Value	Moderate or Severe vs. None: Est. Relative Risk (95% C.I.)[b]	Moderate or Severe vs. None: p-Value
					Analysis Results for Log_2 (Initial Dioxin)[a]			
Low	174	92.0	6.3	1.7	1.05 (0.80,1.37)	0.720	0.80 (0.45,1.43)	0.452
Medium	173	94.2	4.1	1.7				
High	173	92.5	6.4	1.2				

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)[c]				
	Mild vs. None		Moderate or Severe vs. None		
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
520	1.16 (0.85,1.59)	0.353	0.80 (0.36,1.77)	0.574	AGE (p=0.013) BFAT (p=0.056) RACE*PACKYR (p=0.010) OCC*IC (p=0.022)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 20-11. (Continued)
Analysis of Loss of Vital Capacity

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED								
		Percent			Mild vs. None		Moderate or Severe vs. None	
Dioxin Category	n	None	Mild	Mod. or Sev.	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	92.0	6.5	1.5				
Background RH	373	94.1	5.4	0.5	0.94 (0.56,1.57)	0.802	0.41 (0.09,1.79)	0.233
Low RH	260	92.7	5.4	1.9	0.77 (0.43,1.40)	0.397	1.19 (0.43,3.30)	0.738
High RH	260	93.1	5.8	1.2	0.77 (0.43,1.38)	0.384	0.65 (0.19,2.28)	0.504
Low plus High RH	520	92.9	5.6	1.5	0.77 (0.49,1.21)	0.263	0.91 (0.38,2.16)	0.833

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED						
		Mild vs. None		Moderate or Severe vs. None		
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,060					AGE (p<0.001)
						CSMOK (p=0.006)
Background RH	372	0.94 (0.55,1.62)	0.833	0.43 (0.10,1.95)	0.277	BFAT (p=0.007)
Low RH	260	0.67 (0.36,1.23)	0.196	0.97 (0.34,2.77)	0.952	IC (p=0.145)
High RH	260	0.84 (0.46,1.54)	0.582	0.74 (0.20,2.67)	0.643	RACE*PACKYR (p=0.004)
Low plus High RH	520	0.75 (0.47,1.19)	0.220	0.87 (0.36,2.11)	0.754	

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of duty in SEA and change in body fat from the time of duty in SEA to the date of the blood draw for dioxin.
[c] Adjusted for percent body fat at the time of duty in SEA, change in body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin ≤ 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin ≤ 10 ppt, Initial Dioxin > 143 ppt.

Table 20-11. (Continued)
Analysis of Loss of Vital Capacity

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED										
	Current Dioxin Category Summary Statistics					Analysis Results for Log_2 (Current Dioxin + 1)				
			Percent			Mild vs. None		Moderate or Severe vs. None		
Model[a]	Current Dioxin Category	n	None	Mild	Mod. or Sev.	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value	
4	Low	295	94.6	4.7	0.7	1.12 (0.93,1.36)	0.231	1.09 (0.72,1.66)	0.681	
	Medium	299	92.6	6.0	1.3					
	High	299	93.0	5.7	1.3					
5	Low	300	94.7	4.7	0.7	1.13 (0.96,1.34)	0.150	1.08 (0.75,1.56)	0.668	
	Medium	296	92.6	6.1	1.4					
	High	297	92.9	5.7	1.4					
6[c]	Low	299	94.7	4.7	0.7	1.14 (0.95,1.36)	0.151	1.11 (0.76,1.63)	0.584	
	Medium	296	92.6	6.1	1.4					
	High	297	92.9	5.7	1.4					

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 20-11. (Continued)
Analysis of Loss of Vital Capacity

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED						
		Analysis Results for Log_2 (Current Dioxin + 1)				
		Mild vs. None		Moderate or Severe vs. None		
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	892	1.12 (0.90,1.40)**	0.297**	1.05 (0.62,1.78)**	0.852**	CURR*RACE (p=0.019) CURR*CSMOK (p=0.016) AGE (p=0.003) BFAT (p=0.002) RACE*PACKYR (p=0.026)
5	892	1.12 (0.93,1.36)**	0.229**	1.05 (0.67,1.66)**	0.826**	CURR*CSMOK (p=0.049) AGE (p=0.004) BFAT (p=0.003) RACE*PACKYR (p=0.034)
6[c]	891	1.15 (0.94,1.40)	0.187	1.05 (0.64,1.72)	0.839	CSMOK (p=0.067) AGE*BFAT (p=0.040) RACE*PACKYR (p=0.030)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for $\log_2$ total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for $\log_2$ total lipids in addition to covariates specified under "Covariate Remarks" column.

** Log_2 (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); adjustive relative risk, confidence interval, and p-value derived from a model after deletion of this interaction; refer to Appendix Table P-2-7 for further analysis of this interaction.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

age, current cigarette smoking, body fat, industrial chemicals exposure, and a race-by-lifetime cigarette smoking history interaction.

All Model 2 and 3 unadjusted and adjusted analyses of the relationship of loss of vital capacity with initial dioxin were nonsignificant (Table 20-11(c-f): $p>0.19$). Analyses included contrasts between none and mild loss of vital capacity and between none and moderate or severe loss of vital capacity. Age, body fat, and a race-by-lifetime cigarette smoking history interaction were included in both models. Additionally, an occupation-by-industrial chemicals exposure interaction was significant for Model 2, and current cigarette smoking and industrial chemicals exposure were retained in Model 3.

Analysis of current dioxin versus loss of vital capacity proved nonsignificant for all unadjusted and adjusted contrasts examined for Models 4, 5, and 6 (Table 20-11(g,h): $p\geq0.15$ for all contrasts). Adjusted results presented in Table 20-11(h) for Models 4 and 5 are from the final model after significant covariate interactions involving current dioxin were deleted from the model. The current dioxin-by-race and current dioxin-by-current cigarette smoking interactions, as well as age, body fat, and a race-by-lifetime cigarette smoking history interaction exhibited significance in Model 4. A current dioxin-by-current cigarette smoking interaction, a race-by-lifetime cigarette smoking history interaction, age, and body fat displayed significant covariate effects in Model 5. Results stratified by each current dioxin-by-covariate level for Models 4 and 5 are presented in Appendix Table P-2-7. Model 6 was adjusted for current cigarette smoking and age-by-body fat and race-by-lifetime cigarette smoking history interactions. Also, as presented in Appendix Table P-3-9, when body fat was removed from the adjusted model for Models 4, 5, and 6, the positive association between loss of vital capacity for none versus mild becomes significant or marginally significant ($p<0.06$) for all three models.

Obstructive Abnormality

All group differences tested nonsignificant for both the unadjusted and adjusted analyses of obstructive abnormality (Table 20-12(a,b): $p>0.10$ for all contrasts). For the adjusted analysis of obstructive abnormality, the interaction between group and lifetime cigarette smoking history was significant (Table 20-12(b): $p=0.021$). Results stratified by levels of lifetime cigarette smoking history are presented in Appendix Table P-2-8. Results presented in Table 20-12(b) are the adjusted analysis results obtained after excluding this interaction from the model. Other significant effects included age, industrial chemicals exposure, and occupation-by-current cigarette smoking, occupation-by-lifetime cigarette smoking history, and body fat-by-current cigarette smoking interactions.

The unadjusted analysis of Model 2 revealed a significant decreased risk of mild obstructive abnormalities for increasing levels of initial dioxin (Table 20-12(c): $p=0.044$, Est. RR=0.86). However, after adjusting for industrial chemicals exposure and age-by-lifetime cigarette smoking history, current cigarette smoking by-body-fat, and lifetime cigarette smoking history-by-body fat interactions, Model 2 did not detect a significant association between initial dioxin and either of the obstructive abnormalities classifications. For the Model 3 unadjusted analysis, the associations between categorized dioxin and the obstructive abnormalities classifications were nonsignificant (Table 20-12(e): $p>0.13$ for all

Table 20-12.
Analysis of Obstructive Abnormality

a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED

Occupational Category	Group	n	Percent: None	Percent: Mild	Percent: Mod. or Sev.	Mild vs. None: Est. Relative Risk (95% C.I.)	Mild vs. None: p-Value	Moderate or Severe vs. None: Est. Relative Risk (95% C.I.)	Moderate or Severe vs. None: p-Value
All	***Ranch Hand***	***951***	***55.5***	***36.8***	***7.7***	***1.06 (0.89,1.27)***	***0.493***	***1.21 (0.87,1.69)***	***0.256***
	Comparison	***1,280***	***57.5***	***35.9***	***6.6***				
Officer	Ranch Hand	366	51.9	40.7	7.4	1.11 (0.84,1.48)	0.454	1.31 (0.75,2.28)	0.335
	Comparison	502	55.2	38.8	6.0				
Enlisted Flyer	Ranch Hand	162	43.2	44.4	12.4	1.23 (0.80,1.91)	0.344	1.82 (0.88,3.77)	0.106
	Comparison	203	50.2	41.9	7.9				
Enlisted Groundcrew	Ranch Hand	423	63.3	30.5	6.2	0.96 (0.73,1.27)	0.786	0.91 (0.54,1.54)	0.737
	Comparison	575	62.3	31.1	6.6				

b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	Mild vs. None: Adj. Relative Risk (95% C.I.)	Mild vs. None: p-Value	Moderate or Severe vs. None: Adj. Relative Risk (95% C.I.)	Moderate or Severe vs. None: p-Value	Covariate Remarks[a]
All	***1.17 (0.86,1.28)****	***0.624****	***1.05 (0.81,1.69)****	***0.396****	GROUP*PACKYR (p=0.021) AGE (p<0.001) IC (p=0.034) OCC*CSMOK (p=0.011) OCC*PACKYR (p=0.031) CSMOK*BFAT (p=0.002)
Officer	1.08 (0.79,1.47)**	0.638**	1.20 (0.65,2.21)**	0.552**	
Enlisted Flyer	1.24 (0.77,2.01)**	0.379**	1.77 (0.81,3.87)**	0.155**	
Enlisted Groundcrew	0.97 (0.71,1.31)**	0.821**	0.93 (0.53,1.65)**	0.809**	

[a] Covariates and associated p-values correspond to final model based on all participants with available data.

** Group-by-covariate interaction ($0.01 < p \leq 0.05$); relative risk, confidence interval, and p-value derived from a model after deletion of this interaction; refer to Appendix Table P-2-8 for further analysis of this interaction.

Table 20-12. (Continued)
Analysis of Obstructive Abnormality

c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED								
Initial Dioxin Category Summary Statistics					Analysis Results for Log_2 (Initial Dioxin)[a]			
		Percent			Mild vs. None		Moderate or Severe vs. None	
Initial Dioxin Category	n	None	Mild	Mod. or Sev.	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
Low	174	51.2	40.2	8.6	0.86 (0.74,1.00)	0.044	0.80 (0.60,1.06)	0.115
Medium	173	57.8	32.9	9.3				
High	173	68.2	28.3	3.5				

d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED					
Analysis Results for Log_2 (Initial Dioxin)[c]					
	Mild vs. None		Moderate or Severe vs. None		
n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
520	0.98 (0.82,1.16)	0.795	0.97 (0.70,1.34)	0.850	IC (p=0.006) AGE*PACKYR (p=0.036) CSMOK*BFAT (p=0.031) PACKYR*BFAT (p=0.012)

[a] Adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

[b] Relative risk for a twofold increase in initial dioxin.

[c] Adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.

Table 20-12. (Continued)
Analysis of Obstructive Abnormality

e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED								
		Percent			Mild vs. None		Moderate or Severe vs. None	
Dioxin Category	n	None	Mild	Mod. or Sev.	Est. Relative Risk (95% C.I.)[ab]	p-Value	Est. Relative Risk (95% C.I.)[ab]	p-Value
Comparison	1,062	57.5	35.4	7.1				
Background RH	373	51.2	39.9	8.9	1.21 (0.94,1.56)	0.136	1.30 (0.83,2.03)	0.251
Low RH	260	55.0	36.2	8.8	1.08 (0.81,1.45)	0.604	1.29 (0.78,2.14)	0.328
High RH	260	63.1	31.5	5.4	0.85 (0.63,1.14)	0.268	0.74 (0.40,1.35)	0.321
Low plus High RH	520	59.0	33.9	7.1	0.96 (0.76,1.20)	0.701	1.00 (0.66,1.53)	0.987

f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY — ADJUSTED						
		Mild vs. None		Moderate or Severe vs. None		
Dioxin Category	n	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Adj. Relative Risk (95% C.I.)[ac]	p-Value	Covariate Remarks
Comparison	1,060					DXCAT*PACKYR (p=0.026) AGE (p<0.001) OCC*CSMOK (p=0.003) OCC*BFAT (p=0.010) CSMOK*BFAT (p=0.008) BFAT*IC (p=0.037)
Background RH	372	1.14 (0.86,1.51)**	0.360**	1.30 (0.78,2.16)**	0.307**	
Low RH	260	0.96 (0.70,1.32)**	0.822**	1.08 (0.62,1.89)**	0.785**	
High RH	260	1.05 (0.74,1.47)**	0.798**	0.85 (0.44,1.66)**	0.631**	
Low plus High RH	520	1.00 (0.78,1.29)**	0.997**	0.98 (0.62,1.56)**	0.938**	

[a] Relative risk and confidence interval relative to Comparisons.
[b] Adjusted for percent body fat at the time of duty in SEA and change in body fat from the time of duty in SEA to the date of the blood draw for dioxin.
[c] Adjusted for percent body fat at the time of duty in SEA, change in body fat from the time of duty in SEA to the date of the blood draw for dioxin, and covariates specified under "Covariate Remarks" column.

** Categorized dioxin-by-covariate interaction ($0.01 < p \leq 0.05$); adjusted relative risk, confidence interval, and p-value derived from a model after deletion of this interaction; refer to Appendix Table P-2-8 for further analysis of this interaction.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Table 20-12. (Continued)
Analysis of Obstructive Abnormality

g) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — UNADJUSTED									
	Current Dioxin Category Summary Statistics					Analysis Results for Log_2 (Current Dioxin + 1)			
			Percent			Mild vs. None		Moderate or Severe vs. None	
Model[a]	Current Dioxin Category	n	None	Mild	Mod. or Sev.	Est. Relative Risk (95% C.I.)[b]	p-Value	Est. Relative Risk (95% C.I.)[b]	p-Value
4	Low	295	50.5	41.0	8.5	0.84 (0.76,0.92)	<0.001	0.80 (0.67,0.96)	0.015
	Medium	299	53.2	38.1	8.7				
	High	299	63.6	30.1	6.4				
5	Low	300	51.7	40.3	8.0	0.88 (0.81,0.96)	0.003	0.84 (0.72,0.98)	0.022
	Medium	296	52.0	38.5	9.5				
	High	297	63.6	30.3	6.1				
6[c]	Low	299	51.8	40.1	8.0	0.86 (0.79,0.94)	0.001	0.83 (0.71,0.97)	0.018
	Medium	296	52.0	38.5	9.5				
	High	297	63.6	30.3	6.1				

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids.

Note: Model 4: Low = ≤ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = ≤ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

Table 20-12. (Continued)
Analysis of Obstructive Abnormality

h) MODELS 4, 5, AND 6: RANCH HANDS — CURRENT DIOXIN — ADJUSTED						
	Analysis Results for Log_2 (Current Dioxin + 1)					
		Mild vs. None		Moderate or Severe vs. None		
Model[a]	n	Adj. Relative Risk (95% C.I.)[b]	p-Value	Adj. Relative Risk (95% C.I.)[b]	p-Value	Covariate Remarks
4	892	0.88 (0.77,1.01)	0.061	0.86 (0.67,1.09)	0.206	AGE (p<0.001) PACKYR (p<0.001) RACE*IC (p=0.026) OCC*CSMOK (p=0.003) CSMOK*BFAT (p=0.004)
5	892	0.91 (0.82,1.02)	0.123	0.88 (0.72,1.08)	0.228	AGE (p<0.001) PACKYR (p<0.001) RACE*IC (p=0.026) OCC*CSMOK (p=0.003) CSMOK*BFAT (p=0.004)
6[d]	891	0.91 (0.81,1.03)	0.135	0.89 (0.72,1.11)	0.303	PACKYR (p<0.001) AGE*BFAT (p=0.003) RACE*IC (p=0.024) OCC*CSMOK (p=0.003) CSMOK*BFAT (p=0.004)

[a] Model 4: Log_2 (lipid-adjusted current dioxin + 1).
Model 5: Log_2 (whole-weight current dioxin + 1).
Model 6: Log_2 (whole-weight current dioxin + 1), adjusted for log_2 total lipids.

[b] Relative risk for a twofold increase in current dioxin.

[c] Adjusted for log_2 total lipids in addition to covariates specified under "Covariate Remarks" column.

Note: Model 4: Low = $\leq$ 8.1 ppt; Medium = >8.1-20.5 ppt; High = >20.5 ppt.
Models 5 and 6: Low = $\leq$ 46 ppq; Medium = >46-128 ppq; High = >128 ppq.

analyses). Similar, nonsignificant results were found for the adjusted analysis for Model 3 (Table 20-12(f): $p>0.30$ for all contrasts). The adjusted Model 3 analysis detected a significant categorized dioxin-by-lifetime cigarette smoking history interaction (Table 20-12(f): $p=0.026$). Stratified analyses for this interaction are presented in Appendix Table P-2-8. The results presented in Table 20-12 for the adjusted analysis for Model 3 were derived after deletion of the categorized current dioxin-by-lifetime cigarette smoking history interaction. Model 3 was also adjusted for the covariates and interactions of age, occupation-by-current cigarette smoking, occupation-by-body fat, current cigarette smoking-by-body fat, and body fat-by-industrial chemicals exposure.

Each unadjusted analysis of Models 4 through 6 revealed a significant inverse association between obstructive abnormality and current dioxin for the contrasts of mild versus none and moderate or severe versus none (Table 20-12(g): $p \leq 0.022$, Est. RR ≤ 0.88 for all analyses). However, after adjustment for covariate effects for each model, only the mild versus none contrast for Model 4 demonstrated a marginally significant association (Table 20-12(h): $p=0.061$, Est. RR=0.88). When body fat was excluded from the adjusted analysis of Models 4, 5, and 6, the inverse association between current dioxin and mild obstructive abnormalities became significant for all three models (Appendix Table P-3-10(c): $p \leq 0.05$ for all analyses) and marginally significant for the relationship between current dioxin and moderate or severe abnormalities for Models 4 and 5. Significant effects for each model included lifetime cigarette smoking and race-by-industrial chemicals exposure, occupation-by-current cigarette smoking, current cigarette smoking-by-body fat interactions. Age was also significant for Models 4 and 5, and an age-by-body fat interaction was significant for Model 6.

Longitudinal Analysis

Longitudinal analyses were conducted on the ratio of observed FEV_1 to observed FVC to examine whether changes over time differed with respect to group membership (Model 1), initial dioxin (Model 2), and categorized dioxin (Model 3). Models 4, 5, and 6 were not examined in longitudinal analyses because current dioxin, the measure of exposure in these models, changes over time and is not available for all participants for 1982, 1985, or 1992. The longitudinal analyses for this variable investigated the difference between the measures for the 1982 examination and the 1992 examination. Summary statistics for the 1987 examination are provided for reference purposes. This measurement was not collected for the 1985 followup examination.

The longitudinal analysis for the ratio of observed FEV_1 to observed FVC examined the paired difference between the measurements for 1992 and 1982. These paired differences measured the change in the ratio over time. A logarithmic transformation was applied to 1 minus this ratio prior to calculating the paired differences for analysis purposes. Each of the three models used in the longitudinal analysis were adjusted for age and the dependent variable as measured in 1982 (see Statistical Methods, Chapter 7). The analyses of Models 2 and 3 also were adjusted for percent body fat at the time of duty in SEA and change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin.

Laboratory Examination Variable

Ratio of Observed FEV_1 to Observed FVC

The Model 1 analysis of the change in the ratio of observed FEV_1 to observed FVC did not uncover a significant overall difference between Ranch Hands and Comparisons (Table 20-13(a): $p=0.420$). However, stratifying the Model 1 analysis by occupation detected a significant group difference for the enlisted flyers (Table 20-13(a): $p=0.021$). Of the enlisted flyers, the Ranch Hands had an examination mean change of -0.069 between 1992 and 1982, compared to -0.055 for the Comparisons.

The results for the Model 2 analysis did not reveal a significant association between the change in the ratio of observed FEV_1 to observed FVC and initial dioxin (Table 20-13(b): $p=0.374$). Similarly, the Model 3 analysis did not detect a significant relationship between the change in the ratio and categorized dioxin (Table 20-13(c): $p>0.37$ for all contrasts).

DISCUSSION

Although the presence of pulmonary disease may be apparent based on the history and physical examination, definitive diagnosis often requires the collection of laboratory data analyzed in the current section. In addition, because the lung is often involved secondarily in numerous infectious, inflammatory, and neoplastic disorders, the assessment of lung disease should include the type of comprehensive multisystem review conducted in these examinations and reported in other chapters.

Historical information on the occurrence of pulmonary disease must be interpreted with caution in the absence of medical record verification. Many of the cardinal symptoms of lung disease, including dyspnea, chest pain, and exercise intolerance, are common to cardiovascular disease as well (particularly ischemic heart disease) and are misinterpreted frequently as to cause. Wheezing, assumed by the patient to be indicative of asthma, may in fact be reflective of hemodynamic compromise in congestive heart failure. "Pneumonia" and "pneumonitis" are often confused by patients in relating the medical history. Thus, all episodes of pulmonary disease were verified by medical records and only verified occurrences were analyzed.

The physical examination variables studied can provide valuable clues to the presence of pulmonary disease; however, in lacking specificity, these data are limited in confirming a diagnosis. Wheezes and hyperresonance, for example, will occur in obstructive airway disease in asthma or in emphysema secondary to cigarette use. Dullness to percussion, a finding common to many disorders, will occur in consolidation from atelectasis, infections, pleural thickening, or pleural effusion.

In view of the limitations of the history and physical examination noted above, added emphasis is placed on screening laboratory data in the diagnosis of respiratory disease. The chest x ray, when normal, is highly reliable in excluding pulmonary parenchymal disease, though several exceptions must be recognized. Solitary lesions less than 6 millimeters, miliary granulomatous infection, and early interstitial disease, among others, may be present

Table 20-13.
Longitudinal Analysis of Ratio of Observed FEV_1 to Observed FVC

a) MODEL 1: RANCH HANDS VS. COMPARISONS							
		Mean[a]/(n) Examination					
Occupational Category	Group	1982	1987	1992	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
All	***Ranch Hand***	***0.814 (900)***	***0.816 (868)***	***0.761 (900)***	***-0.054***	***-0.002***	***0.420***
	Comparison	***0.815 (1,060)***	***0.817 (1,034)***	***0.763 (1,060)***	***-0.052***		
Officer	Ranch Hand	0.806 (339)	0.809 (333)	0.751 (339)	-0.055	0.000	0.983
	Comparison	0.812 (403)	0.813 (391)	0.757 (403)	-0.055		
Enlisted Flyer	Ranch Hand	0.810 (159)	0.801 (153)	0.742 (159)	-0.069	-0.014	0.021
	Comparison	0.806 (173)	0.805 (172)	0.751 (173)	-0.055		
Enlisted Groundcrew	Ranch Hand	0.822 (402)	0.827 (382)	0.776 (402)	-0.047	0.001	0.798
	Comparison	0.820 (484)	0.285 (471)	0.772 (484)	-0.048		

[a] Transformed from natural logarithm of (1-X) scale.

[b] Difference between 1992 and 1982 examination means after transformation to original scale.

[c] P-value is based on analysis of natural logarithm of 1-ratio; results adjusted for natural logarithm of 1-ratio in 1982 and age in 1992.

Note: Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examination. Data were not collected for the 1985 examination.

Table 20-13. (Continued)
Longitudinal Analysis of Ratio of Observed FEV_1 to Observed FVC

b) MODEL 2: RANCH HANDS — INITIAL DIOXIN					
	Initial Dioxin Category Summary Statistics Mean[a]/(n) Examination			Analysis Results for Log_2 (Initial Dioxin)[b]	
Initial Dioxin	1982	1987	1992	Adj. Slope (Std. Error)	p-Value
Low	0.815 (167)	0.817 (166)	0.759 (167)	-0.0031 (0.0034)	0.374
Medium	0.813 (169)	0.810 (165)	0.757 (169)		
High	0.834 (168)	0.842 (162)	0.792 (168)		

[a] Transformed from natural logarithm of (1-X) scale.

[b] Results based on difference between natural logarithm of 1-ratio in 1992 and natural logarithm of 1-ratio in 1982 versus $\log_2$ (initial dioxin); results adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, natural logarithm of 1-ratio in 1982, and age in 1992.

Note: Low = 39-98 ppt; Medium = >98-232 ppt; High = >232 ppt.
Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Data were not collected for the 1985 examination.

Table 20-13. (Continued)
Longitudinal Analysis of Ratio of Observed FEV_1 to Observed FVC

c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY						
	Mean[a]/(n) Examination					
Dioxin Category	1982	1987	1992	Exam. Mean Change[b]	Difference of Exam. Mean Change	p-Value[c]
Comparison	0.815 (914)	0.817 (904)	0.763 (914)	-0.052		
Background RH	0.804 (341)	0.804 (334)	0.746 (341)	-0.058	-0.007	0.378
Low RH	0.817 (250)	0.816 (248)	0.762 (250)	-0.056	-0.004	0.590
High RH	0.825 (254)	0.831 (245)	0.778 (254)	-0.047	0.005	0.743
Low plus High RH	0.821 (504)	0.823 (493)	0.770 (504)	-0.051	0.001	0.577

[a] Transformed from natural logarithm of (1-X) scale.

[b] Difference between 1992 and 1982 examination means after transformation to original scale.

[c] P-value is based on analysis of natural logarithm of 1-ratio; results adjusted for percent body fat at the time of duty in SEA, change in percent body fat from the time of duty in SEA to the date of the blood draw for dioxin, natural logarithm of 1-ratio in 1982, and age in 1992.

Note: RH = Ranch Hand.
Comparison: Current Dioxin ≤ 10 ppt.
Background (Ranch Hand): Current Dioxin ≤ 10 ppt.
Low (Ranch Hand): Current Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 143 ppt.
High (Ranch Hand): Current Dioxin > 10 ppt, Initial Dioxin > 143 ppt.

Summary statistics for 1987 are provided for reference purposes for participants who attended the Baseline, 1987, and 1992 examinations. Data were not collected for the 1985 examination.

but not detectable radiographically. Furthermore, it is recognized clinically that the chest x ray is not sensitive to the detection of obstructive airway disease in an early stage. On the other hand, the chest x ray may reveal an early occult malignancy in an asymptomatic patient and afford a rare opportunity for cure.

Spirometry has been used as a clinical tool to measure static lung volumes and to detect respiratory disease for more than a century. Dynamic indices, relating changes in lung volume to time, were first developed more than 50 years ago and, with computerization, have been refined to a high degree of accuracy and reproducibility. To be valid, spirometry requires that particular attention be paid to technician training and to eliciting the full cooperation of the patient. In spirometry, a premium is placed on using identical techniques in longitudinal studies. These factors received special emphasis in this study.

The spirometric indices evaluated in this chapter are designed to measure lung volume (FVC) and respiratory air flow (FEV_1). Static lung volume is principally determined by height and is independent of weight, while dynamic volume measurements depend in part on physical strength. Accordingly, all indices require correction for age and height. In the current study, an apparent increase in the FEV_1 to FVC ratio was driven more by a reduction in the static index, FVC, associated with restrictive or infiltrative lung disease, than by any significant changes in the dynamic index, FEV_1.

Respiratory disease may be divided into two general categories in clinical practice. "Restrictive" disease is characterized by reduced vital capacity as seen in interstitial fibrosis or reduced lung volume postsurgical resection. In "obstructive" airways disease associated with cigarette use (usually chronic obstructive pulmonary disease), the flow-dependent index, FEV_1, is abnormally prolonged.

The analyses of dependent variable-covariate associations confirm observations that are well established in clinical practice. Lifetime cigarette smoking history was a highly significant risk factor with respect to the development of bronchitis and pneumonia and for all of the laboratory indices analyzed. Of interest, over the 10-year course of these examinations, the percentage of participants has steadily decreased from 42 percent in 1982 to 25 percent in 1992. Stratification by occupation confirms that, as a group, officers are significantly less likely to develop lung disease than enlisted personnel. With advancing age, an increase in respiratory disease was confirmed by history and on physical examination, as was an age-related decline in the static and dynamic indices of pulmonary function. Related to racial variations in body habitus, Blacks have a slight reduction in vital capacity relative to non-Blacks. Finally, the analyses of body fat confirmed the well-recognized reduction in vital capacity and its derivatives associated with obesity.

The analyses of historical variables yielded inconsistent results. Bronchitis was more common and pneumonia less common in Ranch Hands than in Comparisons. Of interest, but of uncertain cause, Ranch Hand enlisted flyers appeared to be at selective risk relative to Comparisons with respect to the history of bronchitis (19.4% vs. 16.6%) and the frequency of abnormalities noted on physical examination (22.8% vs. 12.3%) and chest x ray (19.1% vs. 14.3%). There was, however, no evidence for any relationship with the current body burden of dioxin.

Although in the analyses of static and dynamic laboratory variables, no significant group differences were defined, within the Ranch Hand cohort there was evidence for a dioxin effect similar to that documented in the 1987 examinations and the subsequent serum dioxin analysis. A slight reduction in FVC was noted in those participants with high versus low extrapolated initial dioxin and in all models employing current serum dioxin as well. Similar directional changes were noted in the FVC derived index of the ratio of observed FEV_1 to observed FVC. Although consistent with a dose-response effect, the differences in the means were slight and of doubtful physiologic significance. Clinically, a reduction in FVC is noted often in obese patients, and these results may reflect in part the strong positive association between current serum dioxin and body fat noted in Chapter 9, General Health.

Longitudinal analyses of the ratio of observed FEV_1 to observed FVC did not reveal any significant differences between the Ranch Hand and Comparison cohorts. In the enlisted flyer category, Ranch Hands had a slightly greater reduction in the ratio than did Comparisons, but the difference (-0.069 vs. -0.055) is not physiologically significant. There was no evidence for any trend in relation to the extrapolated initial or current serum dioxin levels.

In summary, the historical, physical examination, and laboratory data analyzed revealed no evidence for an increase in pulmonary disease in the Ranch Hand cohort relative to the Comparisons. Selected results were consistent with a subtle dose-response effect related to dioxin exposure, although body habitus—and more specifically, body fat—may play a role in these associations.

SUMMARY

The Pulmonary Assessment comprised analyses of the following health endpoints: the occurrence (after duty in SEA) of asthma, bronchitis, and pneumonia; thorax and lung abnormalities; x ray interpretation; FVC (percent of predicted); FEV_1 (percent of predicted); ratio of observed FEV_1 to observed FVC; loss of vital capacity; and obstructive abnormality. Statistical examinations were performed for each variable with group (Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), current lipid-adjusted dioxin (Model 4), and current whole-weight dioxin (Models 5 and 6). Summarized results are presented in Tables 20-14 through 20-17. A summary of group-by-covariate and dioxin-by-covariate interactions is provided in Table 20-18.

Model 1: Group Analysis

The history of bronchitis differed significantly between Ranch Hand and Comparison enlisted flyers for both the Model 1 unadjusted and adjusted analyses ($p=0.037$ and $p=0.033$ respectively), with a higher percentage of enlisted flyer Ranch Hands than enlisted flyer Comparisons having a history of post-SEA bronchitis. Similar results were found for thorax and lung abnormalities. Ranch Hand enlisted flyers exhibited a significantly higher percentage of thorax and lung abnormalities than did Comparison enlisted flyers ($p=0.012$ unadjusted and $p=0.021$ adjusted). In addition, the history of pneumonia differed significantly between groups across all occupations for both the unadjusted and adjusted analyses ($p=0.012$ and $p=0.008$ respectively); however, a higher percentage of Comparisons

Table 20-14.
Summary of Group Analyses (Model 1) for Pulmonary Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Verified Medical Records				
Asthma (D)	NS	NS	ns	NS
Bronchitis (D)	NS*	NS	+0.037	NS
Pneumonia (D)	-0.012	-0.029	NS	ns
Physical Examination				
Thorax and Lung Abnormalities (D)	+0.011	NS	+0.012	NS
Laboratory				
X Ray Interpretation (D)	NS	ns	NS	ns
FVC[a] (C)	ns	ns	NS	ns
FEV_1[a] (C)	ns	ns	ns	ns
Ratio of Observed FEV_1 to Observed FVC[a] (C)	ns	ns	ns	NS
Loss of Vital Capacity[b] (D)	ns	ns	ns*	ns
Loss of Vital Capacity[c] (D)	ns	NS	ns	ns
Obstructive Abnormality[b] (D)	NS	NS	NS	ns
Obstructive Abnormality[c] (D)	NS	NS	NS	ns

[a] Negative difference considered adverse for this variable.
[b] Mild contrasted with none.
[c] Moderate or severe contrasted with none.
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00.
-: Relative risk < 1.00.
NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq0.10$).
Note: P-value given if $p\leq0.05$.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 20-14. (Continued)
Summary of Group Analyses (Model 1) for Pulmonary Variables
(Ranch Hands vs. Comparisons)

Variable	ADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Verified Medical Records				
Asthma (D)	NS	--	--	--
Bronchitis (D)	NS*	ns	+0.033	NS
Pneumonia (D)	-0.008	-0.017	ns	ns*
Physical Examination				
Thorax and Lung Abnormalities (D)	+0.033	NS	+0.021	NS
Laboratory				
X Ray Interpretation (D)	ns	ns	NS	ns
FVC[a] (C)	ns	ns	NS	ns
FEV_1[a] (C)	ns	ns	ns	ns
Ratio of Observed FEV_1 to Observed FVC[a] (C)	ns	ns	ns	NS
Loss of Vital Capacity[b] (D)	ns	ns	-0.048	NS
Loss of Vital Capacity[c] (D)	ns	NS	ns	ns
Obstructive Abnormality[b] (D)	**(NS)	**(NS)	**(NS)	**(ns)
Obstructive Abnormality[c] (D)	**(NS)	**(NS)	**(NS)	**(ns)

[a] Negative difference considered adverse for this variable.
[b] Mild contrasted with none.
[c] Moderate or severe contrasted with none.
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk $\geq$ 1.00.
-: Relative risk < 1.00.
--: Analysis not performed due to sparse number of abnormalities.
NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq0.10$).
**(NS) or **(ns): Group-by-covariate interaction ($p\leq0.05$); not significant when interaction is deleted; refer to Appendix P-2 for further analysis of this interaction.
Note: A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 20-15.
Summary of Initial Dioxin Analyses (Model 2) for Pulmonary Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Verified Medical Records		
Asthma (D)	NS	NS
Bronchitis (D)	NS	NS
Pneumonia (D)	ns	ns
Physical Examination		
Thorax and Lung Abnormalities (D)	NS	NS
Laboratory		
X Ray Interpretation (D)	ns	ns
FVC[a] (C)	ns	-0.034
FEV_1[a] (C)	NS	****
Ratio of Observed FEV_1 to Observed FVC[ab] (C)	+0.008	NS
Loss of Vital Capacity[c] (D)	NS	NS
Loss of Vital Capacity[d] (D)	ns	ns
Obstructive Abnormality[c] (D)	-0.044	ns
Obstructive Abnormality[d] (D)	ns	ns

[a] Negative slope considered adverse for this variable.
[b] Positive association between variable and $\log_2$ (initial dioxin); however, slope is negative in analysis due to natural logarithm (1-X) transformation; directionality of association in table is opposite of analysis slope.
[c] Mild contrasted with none.
[d] Moderate or severe contrasted with none.
C: Continuous analysis.
D: Discrete analysis.
+: Slope negative for variable; however, due to transformation used in analysis, directionality of association is positive.
-: Relative risk < 1.00; slope negative for continuous analysis.
NS or ns: Not significant ($p>0.10$).
**** $\log_2$ (initial dioxin)-by-covariate interaction ($p\leq 0.01$); refer to Appendix P-2 for further analysis of this interaction.
Note: P-value given if $p\leq 0.05$.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis, except as noted above for the ratio of observed FEV_1 to observed FVC.

Table 20-16.
Summary of Categorized Dioxin Analyses (Model 3) for Pulmonary Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED: Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Verified Medical Records				
Asthma (D)	NS	NS	NS	NS
Bronchitis (D)	NS	NS	NS	NS
Pneumonia (D)	ns	ns*	-0.008	-0.002
Physical Examination				
Thorax and Lung Abnormalities (D)	+0.028	NS	NS*	NS
Laboratory				
X Ray Interpretation (D)	NS	ns	ns	ns
FVC[a] (C)	NS	ns	ns	ns*
FEV_1[a] (C)	ns	ns	ns	ns
Ratio of Observed FEV_1 to Observed FVC[a] (C)	-0.009	NS	+0.022	NS
Loss of Vital Capacity[b] (D)	ns	ns	ns	ns
Loss of Vital Capacity[c] (D)	ns	NS	ns	ns
Obstructive Abnormality[b] (D)	NS	NS	ns	ns
Obstructive Abnormality[c] (D)	NS	NS	ns	NS

[a] Negative difference considered adverse for this variable.
[b] Mild contrasted with none.
[c] Moderate or severe contrasted with none.
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk $\geq$ 1.00 for discrete analysis or difference of means nonnegative for continuous analysis.
-: Relative risk < 1.00 for discrete analysis or difference of means negative for continuous analysis.
NS or ns: Not significant ($p>0.10$).
NS* or ns*: Marginally significant ($0.05<p\leq0.10$).
Note: P-value given if $p\leq0.05$.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 20-16. (Continued)
Summary of Categorized Dioxin Analyses (Model 3) for Pulmonary Variables (Ranch Hands vs. Comparisons)

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Verified Medical Records				
Asthma (D)	NS	NS	NS	NS
Bronchitis (D)	+0.036	ns	ns	ns
Pneumonia (D)	ns	-0.038	-0.012	-0.002
Physical Examination				
Thorax and Lung Abnormalities (D)	+0.011	NS	NS	NS
Laboratory				
X Ray Interpretation (D)	**(NS)	**(ns)	**(ns)	**(ns)
FVC[a] (C)	NS	ns	ns	ns
FEV_1[a] (C)	ns	ns	ns	ns
Ratio of Observed FVC to Observed FEV_1[a] (C)	**(ns*)	**(NS)	**(NS)	**(NS)
Loss of Vital Capacity[b] (D)	ns	ns	ns	ns
Loss of Vital Capacity[c] (D)	ns	ns	ns	ns
Obstructive Abnormality[b] (D)	**(NS)	**(ns)	**(NS)	**(NS)
Obstructive Abnormality[c] (D)	**(NS)	**(NS)	**(ns)	**(ns)

[a] Negative difference considered adverse for this variable.
[b] Mild contrasted with none.
[c] Moderate or severe contrasted with none.
C: Continuous analysis.
D: Discrete analysis.
+: Relative risk ≥ 1.00.
-: Relative risk < 1.00.
NS or ns: Not significant (p>0.10).
**(NS) or **(ns): Categorized dioxin-by-covariate interaction (p≤0.05); not significant when interaction is deleted; refer to Appendix P-2 for further analysis of this interaction.
**(ns*): Categorized dioxin-by-covariate interaction (p≤0.05); marginally significant when interaction is deleted; refer to Appendix P-2 for further analysis of this interaction.
Note: P-value given if p≤0.05.
A capital "NS" denotes a relative risk 1.00 or greater for discrete analysis or difference of means nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or difference of means negative for continuous analysis.

Table 20-17.
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Pulmonary Variables (Ranch Hands Only)

	UNADJUSTED		
Variable	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Verified Medical Records			
Asthma (D)	NS	NS	NS
Bronchitis (D)	ns	ns	ns*
Pneumonia (D)	ns	ns	ns
Physical Examination			
Thorax and Lung Abnormalities (D)	ns	ns	ns
Laboratory			
X Ray Interpretation (D)	ns	ns	ns
FVC[a] (C)	-0.002	-0.001	-0.015
FEV_1[a] (C)	NS	NS	NS
Ratio of Observed FEV_1 to Observed FVC[ab] (C)	+<0.001	+<0.001	+<0.001
Loss of Vital Capacity[c] (D)	NS	NS	NS
Loss of Vital Capacity[d] (D)	NS	NS	NS
Obstructive Abnormality[c] (D)	-<0.001	-0.003	-0.001
Obstructive Abnormality[d] (D)	-0.015	-0.022	-0.018

[a] Negative slope considered adverse for this variable.
[b] Positive association between variable and $\log_2$ (current dioxin + 1); however, slope is negative in analysis due to natural logarithm (1-X) transformation; directionality of association in table is opposite of analysis slope.
[c] Mild contrasted with none.
[d] Moderate or severe contrasted with none.
C: Continuous analysis.
D: Discrete analysis.
+: Slope negative for variable; however, due to transformation used in analysis, directionality of association is positive.
-: Relative risk < 1.00 for discrete analysis; slope negative for continuous analysis.
NS or ns: Not significant.
ns*: Marginally significant ($0.05 < p \leq 0.10$).
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or slope nonnegative for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis, except as noted above for the ratio of observed FEV_1 to observed FVC.

Table 20-17. (Continued)
Summary of Current Dioxin Analyses (Models 4, 5, and 6) for Pulmonary Variables (Ranch Hands Only)

Variable	ADJUSTED		
	Model 4: Lipid-Adjusted Current Dioxin	Model 5: Whole-Weight Current Dioxin	Model 6: Whole-Weight Current Dioxin Adjusted for Total Lipids
Verified Medical Records			
Asthma (D)	**(NS)	ns	**(NS)
Bronchitis (D)	**(-0.011)	**(-0.031)	**(-0.004)
Pneumonia (D)	ns*	ns	ns
Physical Examination			
Thorax and Lung Abnormalities (D)	**(ns)	ns	ns
Laboratory			
X Ray Interpretation (D)	****	**(ns)	**(ns*)
FVC[a] (C)	ns	ns	ns
FEV_1[a] (C)	NS	NS	NS
Ratio of Observed FEV_1 to Observed FVC[ab] (C)	+0.001	+0.001	+0.001
Loss of Vital Capacity[c] (D)	**(NS)	**(NS)	NS
Loss of Vital Capacity[d] (D)	**(NS)	**(NS)	NS
Obstructive Abnormality[c] (D)	ns*	ns	ns
Obstructive Abnormality[d] (D)	ns	ns	ns

[a] Negative slope considered adverse for this variable.
[b] Positive association between variable and $\log_2$ (current dioxin + 1); however, slope is negative in analysis due to natural logarithm (1-X) transformation; directionality of association in table is opposite of analysis slope.
[c] Mild contrasted with none.
[d] Moderate or severe contrasted with none.
C: Continuous analysis.
D: Discrete analysis.
+: Slope nonnegative for variable; however due to transformation used in analysis, directionality of association is positive.
-: Relative risk < 1.00.
NS or ns: Not significant.
ns*: Marginally significant ($0.05 < p \leq 0.10$).
**(NS): $\log_2$ (current dioxin)-by-covariate interaction ($p \leq 0.05$); not significant when interaction is deleted; refer to Appendix P-2 for further analysis of this interaction.
**(ns*): $\log_2$ (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); marginally significant when interaction is deleted; refer to Appendix P-2 for further analysis of this interaction.
**(...): $\log_2$ (current dioxin + 1)-by-covariate interaction ($0.01 < p \leq 0.05$); significant when interaction is deleted and p-value given in parentheses; refer to Appendix P-2 for further analysis of this interaction.
**** $\log_2$ (current dioxin + 1)-by-covariate interaction ($p \leq 0.01$); refer to Appendix P-2 for further analysis of this interaction.
Note: P-value given if $p \leq 0.05$.
A capital "NS" denotes a relative risk of 1.00 or greater for discrete analysis or a nonnegative slope for continuous analysis; a lower case "ns" denotes relative risk less than 1.00 for discrete analysis or slope negative for continuous analysis, except as noted above for the ratio of observed FEV_1 to observed FVC.

Table 20-18.
Summary of Group-by-Covariate and Dioxin-by-Covariate Interactions from Adjusted Analyses of Pulmonary Variables

Model	Variable	Covariate
1[a]	Obstructive Abnormality (D)	Lifetime Cigarette Smoking History
2[b]	FEV_1 (C)	Current Cigarette Smoking
3[c]	X Ray Interpretation (D)	Occupation
	Ratio of Observed FEV_1 to Observed FVC (C)	Age
	Obstructive Abnormality (D)	Lifetime Cigarette Smoking History
4[d]	Asthma (D)	Age
	Bronchitis (D)	Industrial Chemicals Exposure
	Thorax and Lung Abnormalities (D)	Current Cigarette Smoking
	X Ray Interpretation (D)	Current Cigarette Smoking
	Loss of Vital Capacity (D)	Race, Current Cigarette Smoking
5[e]	Bronchitis (D)	Industrial Chemicals Exposure
	X Ray Interpretation (D)	Current Cigarette Smoking
	Loss of Vital Capacity (D)	Current Cigarette Smoking
6[f]	Asthma (D)	Age
	Bronchitis (D)	Industrial Chemicals Exposure
	X Ray Interpretation (D)	Current Cigarette Smoking

C: Continuous analysis.
D: Discrete analysis.
[a] Group Analysis (Ranch Hands vs. Comparison).
[b] Ranch Hands—Log_2 (Initial Dioxin).
[c] Categorized Dioxin.
[d] Ranch Hands—Log_2 (Current Lipid-Adjusted Dioxin + 1).
[e] Ranch Hands—Log_2 (Current Whole-Weight Dioxin + 1).
[f] Ranch Hands—Log_2 (Current Whole-Weight Dioxin + 1), Adjusted for Total Lipids.

than Ranch Hands had a history of post-SEA pneumonia. Results are analogous for the officer stratum for the analysis of pneumonia (p=0.029 unadjusted and p=0.017 adjusted). The unadjusted analysis of loss of vital capacity, mild versus none, revealed marginally significant results for enlisted flyers, and the adjusted analysis displayed significant differences. Both analyses showed lower percentages of mild loss of vital capacity for the Ranch Hands than for the Comparisons. The adjusted analysis of obstructive abnormalities revealed a significant interaction between group and lifetime cigarette smoking history.

In the longitudinal analysis, the change in the ratio of observed FEV_1 to observed FVC between 1982 and 1992 differed significantly for enlisted flyers (p=0.021). The ratio decreased, and the change in the ratio was significantly greater for Ranch Hands than for Comparisons.

Model 2: Initial Dioxin Analysis

For the Model 2 unadjusted analyses, significant inverse associations were revealed between initial dioxin and the ratio of observed FEV_1 and observed FVC and mild obstructive abnormalities (p=0.008 and p=0.044 respectively). However, after adjusting for significant covariates, these associations were no longer significant. The adjusted analyses did find a significant association between initial dioxin and FVC (p=0.034). The negative association between dioxin and FVC is indicative of an adverse health effect for increasing levels of dioxin.

Model 3: Categorized Dioxin Analysis

Contrasts involving dioxin measurements on Ranch Hands and Comparisons were examined in the analysis of Model 3. The adjusted analysis of post-SEA bronchitis showed a significantly higher percentage of background Ranch Hands than Comparisons with a history of bronchitis (p=0.036). The unadjusted analysis of post-SEA pneumonia revealed a significantly higher percentage of Comparisons than Ranch Hands in the high and low plus high initial dioxin categories had a history of post-SEA pneumonia (p=0.008 and p=0.002 respectively). After adjustment for covariate effects, the differences remained significant for the high and low plus high categories and also were significant for the low Ranch Hands versus Comparisons, where a higher percentage of Comparisons than Ranch Hands in the low dioxin category had a history of post-SEA pneumonia. For the unadjusted and adjusted analyses of thorax and lung abnormalities, the background Ranch Hands exhibited a significantly higher percentage of thorax and lung abnormalities than the Comparisons (p=0.028 and p=0.011 respectively). The background Ranch Hand and high Ranch Hand contrasts for the unadjusted analysis of the ratio of observed FEV_1 to observed FVC were significant (p=0.009 and p=0.022 respectively). However, after adjusting for covariates, these contrasts were no longer significant.

Models 4, 5, and 6: Current Dioxin Analyses

Current dioxin effects upon pulmonary health variables were analyzed in Models 4 through 6. The adjusted analyses of post-SEA bronchitis revealed a significant inverse association between the history of bronchitis and current dioxin (p=0.011, p=0.031, and p=0.004 respectively). For Models 4, 5, and 6, the analyses of x ray interpretation revealed a significant current dioxin-by-current cigarette smoking interaction. Model 6 revealed a marginally significant association between x ray interpretation and current dioxin after removal of the interaction from the final model. The unadjusted analysis of FVC exhibited a significant inverse association with current dioxin for Models 4 through 6; however, after adjusting for significant covariates, the analyses were no longer significant. The unadjusted and adjusted analyses of the ratio of observed FEV_1 to observed FVC both exhibited highly significant positive associations with current dioxin for Models 4 through 6 ($p \leq 0.001$ for all analyses). This relationship between the ratio and current dioxin could be indicative of a positive health effect; however, the increase in the FEV_1 to FVC ratio as dioxin increases appears to be driven by the significant decrease in FVC for increasing dioxin levels. Unadjusted analyses of obstructive abnormality for Models 4 through 6 each revealed a significant inverse association with current dioxin ($p \leq 0.022$ for all contrasts). However, after adjustment for covariates, only the Model 4 mild versus none contrast remained marginally significant.

CONCLUSION

For the medical records and physical examination pulmonary variables, the group analysis revealed significant relationships for bronchitis and thorax and lung abnormalities only. For enlisted flyers, significantly more Ranch Hands than Comparisons had post-SEA bronchitis and thorax and lung abnormalities. However, the initial dioxin, categorized dioxin, and current dioxin analyses for these variables did not confirm a dioxin dose-response relationship.

For the laboratory variables, a statistically significant inverse relationship was revealed between percent of predicted FVC and initial and current dioxin for Ranch Hands. However, when Ranch Hands were contrasted with Comparisons, no significant differences were detected. Also, the analysis of the ratio of observed FEV_1 to observed FVC within Ranch Hands revealed a significant direct relationship with initial dioxin indicating that the ratio increases (becomes closer to 1) for increasing levels of initial dioxin, which may be due to the diminishing magnitude of FVC in the denominator of the ratio.

In the longitudinal analysis of the ratio of observed FEV_1 to observed FVC, there was a significant group difference for the enlisted flyers. The Ranch Hand enlisted flyers had a larger decrease in the ratio between 1982 and 1992 than the Comparison enlisted flyers.

In summary, the historical, physical examination, and laboratory data analyzed for the Pulmonary Assessment revealed no consistent evidence of an increased prevalence of pulmonary disease in the Ranch Hand cohort in relation to body burden of dioxin.

CHAPTER 20
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